

**A Secondary Data Analysis of Rural African  
Americans and Nonparticipation  
in HIV and AIDS Related  
Clinical Research**

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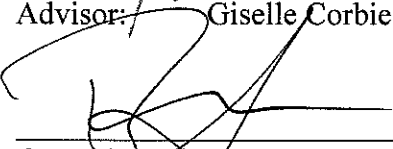
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## Introduction

Human Immunodeficiency Virus (HIV) infection and Autoimmune Immunodeficiency Syndrome have had devastating effects upon the lives and deaths of many across the globe.<sup>1</sup> Within the United States, this epidemic remains an important public health issue. Although advances from medical research have done much to improve the mortality rates and quality of life among those infected, several studies and papers have highlighted an exclusion of U.S. minorities in these studies.

This paper will address several topics regarding HIV/AIDS and U.S. blacks. First of all, the historical impact of HIV/AIDS on the national and state (North Carolina) landscape for the general population will be explored through relevant scientific articles. Patterns of differential incidence, prevalence, mortality, and treatment according to race will also be discussed. These will be covered in the sections:

- HIV/AIDS Morbidity & Mortality
- HIV/AIDS and Race/Ethnicity

Secondly, the inclusion of black U.S. citizens in medical research will be investigated. This will include a short discussion of the importance and implications for inclusion of African Americans in medical research. I will also provide an overview of the existing literature regarding barriers and facilitators for African American participation in general and HIV/AIDS medical research. These will be covered in the section:

- Black Americans and Medical Research

The main scope of this paper, however, is to explore the predictors of research participation among rural African Americans through a secondary data analysis. The former topics are meant to provide the backdrop on which this secondary data analysis will be outlined, discussed, and critiqued. Quantitative data from this small pilot sample will be analyzed, reported, and discussed as is common in the scientific literature. Furthermore, there will be a clear research plan presented for a future qualitative analysis meant to complement our quantitative analyses.

These goals will be met in the following sections:

- Objectives
- Methods
- Results
- Discussion
- Conclusion

## HIV/AIDS Morbidity & Mortality

HIV and AIDS surfaced in the U.S. during the late 1970s – early 1980s. The first five known cases of AIDS in the U.S. were discovered in June 1981.<sup>2</sup> Subsequently, the HIV/AIDS epidemic exploded and peaked during the 1980s and underwent stabilization and some reduction in incidence and mortality rates during the 1990s through the present. Efforts at disease surveillance have resulted in many measurements of incidence and prevalence among different risk groups, with relatively fewer measurements of overall incidence and prevalence among general populations.<sup>3</sup> This section will attempt to provide the best known estimates for the trends of overall incidence, prevalence, and mortality rates for HIV/AIDS in the United States. North Carolina HIV/AIDS epidemiology will also be briefly examined.

### *HIV Incidence*

At present, the best evidence for incidence rates of HIV/AIDS can be found in a systematic review by Vu, Steketee, Valleroy, and colleagues and in national estimates from the Centers for Disease Control and Prevention.

In the afore-mentioned systematic review, the investigators reported HIV incidence rate estimates in Sexually Transmitted Disease (STD) Clinics as 2-3/100 p-y during the late 1980s in Florida and < 1/100 p-y in California in the 1990s.<sup>3</sup> Estimates from STD clinics are limited, however, in that they may represent populations participating in higher risk activities than the general population. Incidence rates may vary by region as well, which limits the ability to draw conclusions of a trend from the studies used in the above systematic review (Table 1).

According to the CDC, an estimated 1.3-1.4 million persons were infected with HIV between 1981 and 2001.<sup>4</sup> Peak HIV incidence is estimated to have been more than 150,000 people per year in the 1980s.<sup>5</sup> Currently, it is estimated that 40,000 new HIV infections have occurred annually since the early 1990s.<sup>6</sup>

### *AIDS Incidence*

An estimated 816,149 AIDS cases have occurred between 1981 and 2001.<sup>6</sup> Incidence rates for AIDS cases peaked in 1993 and have since decreased dramatically (Figure 1).<sup>7</sup> It is thought that the AIDS incidence declined substantially during the late 1990s due to the introduction of combination anti-retroviral therapy.

38% *“From 1995 to 1998, the annual number of incident AIDS cases declined*  
*from 69,242 to 42,832, and deaths from AIDS declined 63% from 51,670*  
*to*

*18,823. The annual number of incident AIDS cases and deaths have remained stable since 1998, at approximately 40,000 and 16,000, respectively.”<sup>6</sup>*

More recently, a 2005 CDC report of HIV/AIDS incidence in 33 states (representing 63% of all cases) reported 157,252 new HIV/AIDS cases from 2001-2004.<sup>8</sup> There was a statistically non-significant decrease in the incidence rate, 22.8 per 100,000 in 2001 to 20.7 per 100,000 in 2004. Caution must be used in interpreting their reported trend, however. First of all, the CDC launched their Advancing HIV Prevention (AHP) initiative in 2003. This may have resulted in increased testing, which would inflate the 2003-2004 incidence rates. Second of all, this report does not include data from California, among other states. The large population and unique demographics among those infected with HIV in California and other states could conceivably change their incidence estimates significantly.

#### *HIV/AIDS Prevalence*

A cross-sectional study examined HIV prevalence within four different counties in the Western U.S. for 1989-1990<sup>9</sup>. HIV prevalence was reported as ~2% in STD clinics in all counties except for San Francisco, for which it was reported at 9.3%. This was a fair quality study limited by potential for measurement and selection bias. This study also lacks generalizability to national populations because of demographic characteristics specific to the Western U.S. (Table 2).

Another study examining HIV prevalence rates during 1989-1990 focused on HIV-1 infection among those 15-49 years of age seeking care from primary health care providers in a nation-wide sample population (n=9,076).<sup>10</sup> They report an overall prevalence rate of 2.3/1000 (95% CI 1.3-3.3). In addition, there was a prevalence rate of 1.0/1000 (95% CI 0.3-1.7) for previously undiagnosed HIV-1 infection. Men were found to have an HIV-1 prevalence four times that of women, and non-rural practices to have a prevalence rate three times that of rural practices. This study was of good quality and presents results consistent with the current literature for that time period, as cited by the authors. This study can not be generalized to broad populations, however, because not everyone in general populations seeks care. Furthermore, their generalizability is limited by the age parameters of the sample and the racial composition, which is not nationally representative (Table 3).

The CDC estimated HIV cases for 1986 and 1989 to be 750,000 and 1 million, respectively. Given the census population estimates for those years, a rough estimation of prevalence for those years is 0.31% and 0.41% respectively.<sup>11, 12</sup>

More recently, several investigators have attempted to measure HIV prevalence in primary care practices. Specifically, a cross-sectional study conducted in 2000 measured prevalence of acute HIV infection among patients with symptoms of a viral illness who presented to an urgent care center at an urban teaching hospital

from March 30, 2000 to March 30, 2001.<sup>13</sup> They reported total HIV prevalence as 2.2% (95% CI 0.9-3.5), acute HIV prevalence as 1.0% (95% CI 0.1-1.9), and chronic HIV prevalence as 1.2% (95% CI 0.2-2.2). This study was of good quality, had patient demographics similar to 72 other hospitals in the U.S., and reported prevalence estimates similar to those previously reported (Table 4).

Another cross-sectional study conducted in 2000 measured prevalence of acute HIV infection in patients visiting physicians' offices, emergency departments, and hospital outpatient clinics.<sup>14</sup> All patients included in the study had symptoms consistent with primary HIV infection. They found those presenting with fever, rash, or pharyngitis to have HIV prevalence estimates of 0.66% (95% CI 0.53-0.92), 0.56% (95% CI 0.35-0.94), and 0.13% (95% CI 0.10-0.19), respectively. The overall quality of this study is good, but it is not generalizable to those >54 years of age, federal, veteran, and military outpatient facilities, and those w/ undiagnosed chronic HIV infection (Table 5).

The CDC estimates that 850,000--950,000 were living with HIV in 2002. Of these, approximately 25% were unaware of their serostatus.<sup>6</sup> The prevalence of AIDS has also risen dramatically since the late 1980's (Figure 2)(Figure 3). The HIV prevalence rate reported for 2004 by the CDC was 168.8 per 100,000 people (Figure 4).

In short, HIV prevalence estimates vary depending on the population studied and the methods used. Despite this limitation, the afore-mentioned studies suggest a continuing HIV epidemic that is of profound public health importance within the U.S. Efforts aimed at slowing this epidemic have stabilized HIV incidence, but improved HIV/AIDS therapy are prolonging the lives of those infected. Thus, the number of those living with HIV/AIDS is increasing.

#### *HIV/AIDS Mortality*

From 1981-2001, the CDC estimates that 467,910 deaths occurred from HIV/AIDS.<sup>6</sup> Mortality from HIV/AIDS rose steadily during the 1980's and peaked in 1995 at ~55,000 per year (Figure 3)(Figure 5). From 1995 to 1998, the deaths from AIDS declined 63% from 51,670 to 18,823 annually. The annual number of deaths have remained stable since 1998, at approximately 16,000 per year.<sup>15</sup> A similar trend is observed when analyzing potential years of life lost from HIV (Figure 6).

#### *HIV/AIDS Epidemiology in North Carolina*

Similar to the national landscape, HIV and AIDS has become a serious problem in North Carolina as well. In 2004, N.C. reported 1,099 incident cases of HIV, as well as an HIV prevalence rate, and AIDS prevalence rate higher than many other states in the U.S. (Figure 4)(Figure 7)(Figure 8).

N.C. HIV incidence was first seen to increase in 1990 after the institution of state-required HIV infection reporting (Figure 9). Although HIV incidence in N.C. has decreased since its peak in the mid-1990's, incidence rates have recently appeared to increase again. This is thought to be from new surveillance methods that have added older prevalent cases to the system.<sup>16</sup> HIV and AIDS prevalence in North Carolina has also been reported as increasing as recent as 2004 (Figure 10).

Lastly, there were 454 HIV/AIDS deaths reported in N.C. for 2003, which is 30 less than in 2002.<sup>16</sup> It was ranked as the 8<sup>th</sup> and 7<sup>th</sup> leading causes of death for North Carolinians in the 15-24 and 25-44 age groups, respectively.

## HIV/AIDS and Race/Ethnicity

### *National Disparities in Epidemiology*

The early AIDS epidemic was characterized very strongly by race and transmission category. The CDC reports that in 1985, ~60% and ~65% of all new AIDS cases were among white Americans and men who have sex with men (MSM), respectively (Figure 11)(Figure 12). In addition to the large burden of AIDS among whites, other epidemiological measures of frequency indicated a growing inclusion of African Americans among the number infected.

According to a fair quality systematic review exploring the extent of HIV/AIDS infections among black Americans, the estimated seroincidence for HIV from 1985 – 1991 was 51.1 vs. 3.7 per 100,000 p-y for black and white Americans, respectively.<sup>17</sup> They further report seroprevalence from 1988 – 1994 as 1.10% and 0.20% for black and white Americans ages 18-59, respectively. Thus, increasing numbers of African Americans were contracting HIV during the late 1980s and early 90s.

Since ~ 1994, black Americans have comprised a larger proportion of AIDS cases than white Americans (Figure 11). In 1998, black and white Americans were 45.1% and 33.4% of all incident AIDS cases, respectively (Table 6). 1996 unpublished CDC data reported by Smith and colleagues cites the HIV seroprevalence for black and white men age 16-21 as 0.22% and 0.04%, respectively. The 1996 HIV seroprevalence for black and white women age 16-21 was reported as 0.35% and 0.07%, respectively. Similar patterns may be seen in a 1998 estimation of HIV and AIDS incidence and prevalence (Table 7).<sup>18</sup>

More recent examinations of HIV/AIDS demographic distributions continue to show similar trends. 2003 HIV/AIDS diagnosis rates were estimated as 74 and 9 per 100,000 for blacks and whites, respectively (Table 8).<sup>2</sup> At the end of 2003, 48% of the HIV/AIDS cases were African Americans. The prevalence rate reported was 114 vs. 765 per 100,000 for white and black Americans, respectively. This data is limited by the inclusion of only the 32 states for which name-based reporting was available. The 2004 data, with the inclusion of New York, continued to show similar patterns (Table 9)(Figure 13)(Figure 14).<sup>8</sup> While the absence of data from other important states such as California certainly makes these reports less than ideal, they provide fair evidence for the continuing disproportionate burden of HIV and AIDS among the black community.

### *N.C. Disparities in Epidemiology*

Within North Carolina, there were 1,641 new HIV diagnoses in 2004.<sup>16</sup> 1,081 (66%) of these were among blacks. The incidence rates of HIV in N.C. were reported as 58.9 and 7.6 per 100,000 for blacks and whites, respectively. Overall, blacks made up 71% of the 17,960 individuals in N.C. living with HIV or AIDS in 2004.

### *National Disparities in HIV/AIDS Mortality*

In addition to African Americans acquiring HIV at an alarmingly high rate and comprising a higher proportion of the HIV and AIDS cases than white Americans, the HIV/AIDS epidemic has taken a large toll on black mortality rates. The HIV/AIDS estimated mortality rate for 1998 was 58.2 and 9.8 per 100,000 for black & white men, aged 25-44, respectively.<sup>17</sup> The estimated mortality rate for women was 25.6 and 1.9 per 100,000 for blacks & whites, aged 25-44, respectively.

In 2005, the HIV/AIDS Surveillance Report released data regarding survival time after AIDS diagnosis for 2000.<sup>19</sup> American Indians/Native Alaskans had the highest percentage of AIDS diagnoses surviving after 12, 24, and 36 months: 92%, 89%, and 85%, respectively. Whites were reported as 91%, 87%, and 85%, respectively. 90%, 85%, and 81% of blacks survived for 12, 24, and 36 months, respectively.

As recently as 2003, the CDC continued to report HIV mortality data for African Americans that was consistently higher than that of other races (Figure 15)(Figure 16). Their report of mortality rates by race shows an approximate seven-fold difference between black Americans and white Americans. In addition, the estimated potential life years lost from HIV for blacks has and continues to be at least seven times greater than that for whites (Figure 17). HIV has been estimated to account for 11.2% of the racial disparity in potential life-years lost from all causes.<sup>20</sup>

### *N.C. Disparities in HIV/AIDS Mortality*

North Carolina surveillance data indicates large differences in deaths attributable to HIV and/or AIDS according to race. There were 453 such deaths in N.C. in 2003.<sup>16</sup> 74% of these were among blacks, while only 23% were in whites. This distribution was similar when stratified by sex. The crude death rates for blacks and whites were 18.2 and 1.7 per 100,000, respectively. This large difference in crude death rates was also seen when stratified by sex. Reported death rates for males were significantly higher than those for females, however.

Similar to national HIV/AIDS reporting practices, survival data for AIDS diagnoses for the year 2001 have been released.<sup>16</sup> 86.4%, 81.6%, and 81.0% of whites' AIDS cases were alive at 12, 24, and 36 months after their diagnosis, respectively. Blacks' AIDS cases survived at 89.7%, 85.0%, and 82.3% for 12, 24, and 36 months, respectively.

Thus, it appears that the proportion of black AIDS patients surviving over time is equivalent to, if not better than, that of white AIDS patients in N.C. These data are a notable improvement from the N.C. 1998 data, in which greater proportions of white AIDS patients were surviving than black AIDS patients. Thus, it appears that NC AIDS care is improving for black Americans.



The afore-mentioned pattern also shows 2001 N.C. black AIDS patients as surviving at equal or greater proportions than U.S. black AIDS patients in 2000 at 24 and 36 months after diagnosis. This may represent better AIDS care in N.C. than in the U.S. as a whole. Alternatively, this may only be an improvement seen over time that would also be present in national 2001 data, were it available.

The discrepancy between the mortality rates and survival proportions may be partially accounted for by the HIV attributable deaths not included in the proportion data. There may also be a significant number of African Americans with HIV/AIDS who are outside of the healthcare system. Thus, they may not be diagnosed until they are at or near death. In such cases, only approximately one third of such individuals would be captured in a three-year follow-up of survival when restricting date of diagnosis to the first year only.

#### *National Disparities in HIV/AIDS Care*

The 2002 Institute of Medicine Report on Health Care disparities acknowledges that U.S. minority populations are less likely to receive appropriate HIV/AIDS care than non-minority patients.<sup>21</sup> It further reports that minority patients receive poorer quality HIV/AIDS care than non-minority patients, even when access to care is equivalent. A recent presentation by a well-known HIV/AIDS researcher similarly suggested that the specific racial disparities in HIV/AIDS care are currently recognized as problems obtaining HIV care and differential quality of HIV care.<sup>22</sup>

#### *Problems Obtaining HIV/AIDS Care*

Black Americans are disproportionately infected with HIV. Despite the gross imbalance of HIV incidence and prevalence between racial groups, a nationally representative sample of all persons receiving HIV/AIDS care in 1999 found only 33% of those receiving care to be Non-Hispanic blacks.<sup>23</sup> Approximately 48% of HIV/AIDS cases are estimated to be black Americans.<sup>2</sup>

In addition to the overall inadequate acquisition of HIV care by African Americans, there is also evidence that receipt of such care may be delayed differently according to race. Turner and colleagues report such an observation in a retrospective cohort study measuring time to receipt of first HIV medical care from the initial date of diagnosis in a national probability sample.<sup>24</sup> They report African Americans as having 1.56 times the odds (95% CI 1.19-2.04) of having their HIV care delayed >3 months compared to white Americans, after adjustment for several health care delivery, demographic, and socio-economic factors. Of all patients with delayed care for >3 months, the median delay time was 1 year. Although this study is of overall good quality, it does feature inadequate measurement of patient trust and thus potential confounding from patient trust issues, as well as patient satisfaction and patient-provider communication. This data also represents trends recorded in 1996, which may not be relevant today.

The best evidence concerning HIV care disparities, however, is from a systematic review performed by Palacio and colleagues.<sup>25</sup> Their analysis of 28 studies spanning from 1984 to 1999 found 14 studies with a negative association, three with a positive association, and 12 with no association between race and HIV treatment. Seven studies also had mixed results across several measures of HIV treatment. Their critical analysis of these studies led to their conclusion that the overall evidence for racial disparities in HIV care is strong. This paper did not, however, document any attempt to acquire unpublished data to reduce publication bias.

#### *Differential Quality of HIV/AIDS Care*

In 1999, Shapiro and colleagues reported on several quality of care measures in a retrospective, nationally representative sample of HIV/AIDS patients.<sup>26</sup> At baseline, blacks had greater odds than whites of having <2 Outpatient visits in six months (OR = 1.49; 95% CI 1.06-2.09) and  $\geq 1$  Emergency Department visit without associated hospitalization in six months (OR=1.72; 95% CI 1.23-2.13) after adjustment for CD4 count, age, sex, exposure, insurance, education, and geographic region. This adjusted model also showed blacks to have greater odds of not receiving ART (OR=2.16; 95% CI 1.54-3.05) and not receiving PCP prophylaxis (OR=1.54; 95% CI 1.03-2.29) than whites. These differences were not statistically significant after a median 15 month follow-up. The investigators did show, however, differential lag times for dissemination of newer antiretroviral medications by race. Blacks waited a mean of 13.5 months while whites waited 10.6 months ( $p < 0.001$ ). This raises the concern that these treatment disparities are not improving over time, but merely shifting to newer treatments. That is, as disadvantaged groups fully acquire yesterday's standard of care, the advantaged move on to the new standard of care. This study is of good quality and generalizable to the entire U.S., but uses sampling methods which may not include those with very poor access, the very healthy, and the less compliant.

A later study of racial disparities in receipt of HAART reports a similar trend for receipt of HAART.<sup>27</sup> Gebo and colleagues report African Americans as receiving HAART less often than white Americans (OR=0.84, 95% CI 0.73-0.96), even when adjusted for access to care, IV drug use, disease severity upon diagnosis, and other demographic variables. This suggests that mere availability of HIV care does not fully account for the treatment disparities reported. The quality of the HIV care may be sub-optimal. This retrospective cohort is of fair quality and limited by potential confounding from socioeconomic status and possible medical or patient reasons for not receiving HAART. In addition, these results do not generalize nationally, nor to all HIV care sites, because the sample is not nationally representative and the participating sites were all highly experienced in HIV/AIDS treatment.

In 2003, Ghani and Anderson reported on receipt of HAART within the HIV Insight™ (APACHE) database.<sup>28</sup> This database is comprised of U.S. HIV patients receiving outpatient care in various non-disclosed locations. African

Americans were less likely to receive HAART as their first ART than whites (OR=0.59; 95% CI 0.50-0.71) when adjusted for age and year of starting ART. Although this fair quality evidence supports previous findings, the limited information on demographics and sampling design limits external validity and introduces potential for selection bias. In addition, various regional characteristics, patient characteristics, physician characteristics, and disease status may all confound the relationship between race and receipt of HAART as their first ART.

#### *Possible Explanations for the HIV Care Disparity*

Several studies have explored possible explanations for HIV treatment disparities. Inadequate HIV testing rates has been proposed as a potential barrier. Failure to diagnose HIV seropositive individuals precludes receipt of proper care. A greater proportion of African Americans, however, receive HIV testing than white Americans.<sup>29</sup> Although notable, an estimated 25% of prevalent HIV cases in 2002 were not aware of their serostatus.<sup>6</sup> It is possible that blacks are disproportionately represented among the 25% who are unaware. In such a case, the higher testing rates among blacks, which are far from 100%, may not be enough to identify and lead equitable numbers of infected blacks to seek proper medical care.<sup>29</sup> In addition, the unaware HIV positive blacks may be unmeasured or unsampled in studies of incidence/prevalence, but represented in the data currently supporting disparities in access to HIV care. In short, the 25% whom are unaware of having HIV may be accounting for the difference in treatment rates.

In addition, fear of a positive HIV test result may deter individuals from seeking HIV testing. Ebrahim et al. hypothesizes that knowledge of HIV treatments may decrease such fear.<sup>29</sup> Their survey showed blacks to have lower odds of knowing that HIV/AIDS treatment exists than whites (OR = 0.58, 95% CI 0.51-0.66). Thus, a difference in HIV knowledge between racial groups may play a role in the disparity in HIV treatment.

In the fore mentioned retrospective cohort from Shapiro and colleagues, blacks were found to have statistically significant poorer quality of care than whites in four of six measures.<sup>26</sup> The authors noted, however, that the addition of insurance to their statistical models attenuated the association between race and the six quality measures considerably. Thus, possession and type of insurance may play a significant role in the racial disparity in HIV treatment.

Provider mediated delay of antiretroviral treatment because of concerns about patient adherence has also been explored. A good quality prospective cohort study found that blacks received protease inhibitors later than whites, regardless of providers' "prescribing attitudes."<sup>30</sup> Furthermore, providers have been shown to inadequately discern which patients will be adherent to antiretroviral therapy.<sup>31-</sup>  
<sup>33</sup> Given the recent evidence of no association between being African American and becoming less adherent for all who were initially 100% adherent (p=0.26), it

is unethical for providers to withhold treatment based on race.<sup>34</sup> Further investigation for predictors of becoming less adherent over time in blacks may provide more insight into this issue.

Blacks have also been shown to have unequal access to providers with HIV-related expertise. Heslin and colleagues report blacks as having lower odds of having an infectious disease specialist for their HIV care than whites (OR=0.60, 95% CI 0.37-0.95), but no difference in provider HIV patient volume (OR=0.93, 95% CI 0.77-1.11).<sup>35</sup> While of fair quality, this study does not account for physician knowledge. In addition, the specialty and HIV patient volume, which were modeled separately but are conceivable related, were not covariates in each others' model. The results remain important, however, because specialty training and experience (HIV case load and years in medical practice) are associated with choosing guideline-concordant treatment regimens.<sup>36</sup>

Lastly, racial concordance between patient and provider has been explored for an association with time to receipt of protease inhibitors. Using a nationally representative sample, King and colleagues report that white patients with white providers receive protease inhibitors sooner (median 278 days) than black patients with black providers (median 419 days;  $p<0.01$ ) and black patients with white providers (median 443 days;  $p<0.001$ ). Furthermore, after adjustment for patient and provider characteristics and provider attitudes, blacks with same race providers received protease inhibitors sooner than whites with same race providers ( $p<0.05$ ) while blacks with white providers received protease inhibitors later than whites with same race providers ( $p<0.05$ ). Limitations for this fair quality study include non-differential measurement biases such as inadequate measurement of trust and recall bias, selection bias through exclusion of 9% of sample who could not identify an HIV care provider, and potential confounders such as regional standard of care, patient participation with provider, patient-physician communication, and several domains of trust that were not measured.

## **Black Americans and Medical Research**

### *Black Americans Underrepresented in HIV Research*

Black Americans are disproportionately infected with HIV and AIDS. Recent data shows blacks to comprise a large portion of incident and prevalent HIV and AIDS cases (Figure 11)(Figure 13)(Figure 14).<sup>2,8</sup> In addition, affected blacks have mortality rates and estimated potential life-years lost ~10 and ~6 times greater than whites, respectively (Figure 15)(Figure 17). Even treatment for HIV and AIDS is utilized differentially between races in the U.S.<sup>21</sup>

Despite these staggering inequalities, much of the HIV targeted research does not include adequate representation from those who are affected most by this illness: black Americans.<sup>37</sup> In fact, this is true of blacks' enrollment in research trials for several diseases, including diabetes, cardiovascular disease, HIV/AIDS, and cancer, among others.<sup>38,39</sup> The following sections will concentrate on:

1. A brief overview of blacks' nonparticipation in all research trials.
2. Barriers for blacks' nonparticipation in all research trials.
3. Barriers for HIV/AIDS trials, specifically.

### *Background: Nonparticipation of black Americans in Clinical Research*

In 1972, one of the most well-known examples of unethical research came to light: the Tuskegee Syphilis Study.<sup>40</sup> The United States Public Health Service observed the natural history of untreated syphilis in 400 black men in Macon County, AL. These men were told they were receiving treatment when in fact they were not. This continued until 1972 despite the availability of bismuth and arsenic, and the later discovery of penicillin, as effective treatment for syphilis. More than 100 men participating in this study succumbed to syphilis and its complications.

This widely publicized breach of research ethics led to considerable changes, such as the creation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and the National Research Act. Subsequent changes involved stronger protection of vulnerable populations and ensuring that risks and benefits associated with clinical research are minimized and maximized, respectively. Institutional Review Boards have served as one means to that end.

After these changes, inclusion of minorities in clinical research became unusual.<sup>40</sup> This transition to an opposite extreme has several fallacies. First of all, disproportionate research inclusion violates the bioethical principle of justice. In short, all risks and benefits of clinical trials should be evenly distributed among individuals, communities, and society.<sup>41</sup> Presently, whites undertake disproportionately higher risks and receive disproportionately more benefit from medical research, as compared to blacks.

In addition, research subjects must be representative of their general population to ensure generalizability to society. When representative samples are not used, potential differences in efficacy and/or effectiveness of interventions by omitted demographic groups may go undiscovered.<sup>39, 42</sup> This results in treatments developed for only certain segments of our population.

Increased awareness of race and sex-based omissions in research inclusion led to the NIH Revitalization Act of 1993.<sup>40</sup> This legislation mandated that minorities and women all be included in clinical research unless there are strong reasons for their exclusion. The goals of minority inclusion in research have since been further clarified and summarized by one researcher as:

1. Generating hypotheses about possible differences by race.
2. Testing hypotheses of differences by race.
3. Ensuring fair and unbiased sharing of the risks and benefits of research participation.<sup>43</sup>

Although these ideals have been embraced by funding agencies such as the NIH, investigators have not uniformly changed reporting practices for clinical research. In a good quality systematic review, Corbie-Smith and colleagues examined reporting practices in three widely known and read general medicine journals, *Annals of Internal Medicine*, *JAMA*, and *New England Journal of Medicine*, for four diseases with established disparities based on race. Of 253 articles from 1989 to 2000, 98% of these did not focus on a single race and 41% of these did not report the race/ethnicity of their study participants. In addition, when considering year of publication, year that recruitment started, the disease studied, and funding source, only the disease being studied was significantly associated with race reporting (OR=3.7; 95% CI 2.0-6.8). Although this study has good internal validity, some assessment of confounding by specific journal, sample size of study, or race of investigators or editors, if feasible, would have added further insight to their results. Furthermore, their generalizability is limited by inclusion of only three journals and only four diseases. These journals do, however, reach very wide audiences.

Corbie-Smith's finding that year of publication was not associated with reporting race is especially disturbing given that previously mentioned ethical guidelines and well known reporting guidelines, such as the CONSORT statement, were published in the mid-90's. In 2001, the NIH revised their guidelines on minority research inclusion to stress subgroup analyses when prior evidence suggest differences by race or ethnicity.<sup>44</sup>

#### *Barriers for Participation in Clinical Research*

Investigations regarding nonparticipation in clinical research are well represented in the literature. Of particular interest is a fairly recent systematic review of patient and physician barriers to participation in randomized trials (Table 10).<sup>45</sup> From an extensive literature search of Medline, Embase, and CINAHL from 1986 to 1996, they identified 78 eligible papers. Potential barriers to patients were

identified as patient concerns such as additional demands on patient, patient preferences for a particular treatment, worry about uncertainty of treatment or trials, and patient concerns about information and consent. Physician concerns hindering patient participation were protocol causing problems with recruitment, clinician concerns about information provision to patients, and clinician influencing patient decision not to join.

This paper is notable within this discussion, however, not for what it reports, but for what it does not report. There is no mention, stratification, or other such analysis by race within this paper. Of the 78 eligible papers summarized, only three can be identified as targeting ethnic minorities from their titles or study descriptions. Given the past severe exclusion of blacks in research, it is unlikely that the other 75 studies account for a proportion of blacks proportionate to those who are targeted for research participation.

#### *Barriers for black Americans' Participation in Clinical Research*

Recruitment of minorities for clinical research has proven to be difficult for investigators.<sup>46</sup> Efforts successful for enlisting white participants may not work as well for blacks.<sup>47</sup> This has motivated several researchers to investigate the barriers, facilitators, and solutions to research participation among African Americans.<sup>37, 42, 46, 48-51</sup> The remainder of this discussion will focus on the reported barriers in such studies.

A relatively older qualitative study used telephone interviews in 1993 to generate hypotheses about why African Americans do not participate in clinical research in Buffalo, NY. Eight African Americans reported "fear", "lack of information," "mistrust of being treated like guinea pigs," and "mistrust of white people."<sup>42</sup>

Another qualitative study utilized focus groups in 1997 to generate hypotheses about barriers clinical research among blacks in Atlanta, GA.<sup>48</sup> After reaching saturation, Corbie-Smith and colleagues report five focus groups as indicating mistrust, inconvenience, too much risk, fear of injections and needles, concerns about physicians being fully honest about risks and procedures, no need because of current good health, and non-sharing of final research benefits with the black community as being deterrents to their participation in clinical research. The groups also identified the Tuskegee study as justification for their mistrust regarding researcher dishonesty and non-beneficence. The internal validity for this study was strong. These results are also most generalizable to women, the poor, and the uninsured.

A third qualitative study investigating perceptions of clinical research recruited 60 African Americans from Los Angeles, Chicago, Washington, D.C., and Atlanta for participation in seven focus groups (Table 11).<sup>46</sup> Barriers reported for these groups were distrust of white researchers, privacy, full awareness of treatment allocation, and the high risk. Some groups did, however, distinguish between non-invasive research (ex. surveys, focus groups, etc.), which was more

acceptable, versus research involving invasive interventions (ex. medications, surgeries, etc.). Although the researchers do not report reaching saturation, their methods suggest strong internal validity and improved external validity in comparison to the previously mentioned qualitative studies.

A recent analysis of four focus groups composed of staff, students, and faculty from the University of Minnesota Twin Cities campus investigated factors that impede research participation among minorities.<sup>50</sup> Comprised of ~56% African Americans, these groups most often identified limited knowledge about health studies, limited community involvement in the design of studies, use of invasive procedures, and mistrust of researchers as potential impediments. The Tuskegee study was also brought up by five of the 10 African Americans as a potential barrier. This study is limited by poor explanations of their selection process, and measurement and analysis techniques. The participants were also considerably homogenous regarding higher education, female sex, highly health conscious, and geographic region. This study represents fair quality internal and external validity.

Regarding quantitative research, Shavers and colleagues examined whether differences of prevalence of socio-cultural beliefs accounted for the difference in willingness of African Americans to participate in research (Table 12).<sup>51</sup> With multivariate modeling, knowledge of the Tuskegee Study and changes in trust resulting from knowledge of the Tuskegee study predicted African American willingness to participate in clinical research. In contrast, educational level and beliefs regarding the racial sharing of medical research risks predicted the willingness of white Americans to participate in clinical research. Lastly, the authors concluded that “the role of Tuskegee appears to lie with its contribution to the overall distrust of medical research among African Americans.”<sup>51</sup> This last observation mirrors that made by Corbie-Smith and colleagues in their fore-mentioned qualitative analysis.<sup>48</sup>

Although Shavers and colleagues present thought provoking results, their internal validity is weakened by reporting inconsistencies within this publication as well as with their previous publication reporting only results for African Americans, questionable statistical methodology, differential non-coverage bias, only a 36% response rate, and non-differential measurement bias from two different survey techniques.<sup>51, 52</sup>

In 2002, Corbie-Smith and colleagues tested a previously generated hypothesis regarding the association between race and trust regarding clinical research (Table 13).<sup>53</sup> After controlling for education, employment, and geographic region, blacks race was significantly associated with having more distrust (OR=4.7; 95% CI 2.9-7.7). Mild selection bias may have occurred from requiring the possession of a telephone. Thus, those at the lowest and highest extremes of SES may have been excluded through not having a phone and being too busy, respectively. Although sex was significantly related to the outcome, distrust ( $p=0.02$ ), it was



not included in the model because there was not a statistically significant association with the exposure, race ( $p=0.14$ ). This author questions the appropriateness of that decision and considers sex a potential confounder. Overall, however, this study exhibits good internal validity and results likely generalizable to the entire U.S. population.

*Barriers for black Americans' Participation in HIV/AIDS Clinical Research*

Consistent with the increase in research regarding barriers to minority participation in all clinical research, there have also been several such trials dealing with HIV/AIDS trials specifically. One such cross-sectional survey administered between 1993 and 1994 measured participation rates by sex and explored differences in reasons for non-participation by various demographics (Table 14).<sup>54</sup> Whites were found to participate at higher rates than persons of color (OR=2.14; 95% CI 1.12-4.08) after adjusted for disease severity, age, education, and clinic type. For non-participants, the most common reasons cited were not informed about trials (28%), not interested or did not want to (28%), fear of experimentation (20%), and not eligible (14%). When stratified by race, Persons of color were significantly more likely to report no interest (31.9% vs. 16.4%,  $p<0.05$ ) and less likely to report not eligible (10.4% vs. 22.4%,  $p<0.05$ ). This study is limited to fair internal validity from potential confounding and measurement bias from racial concordance of study interviewer, confounding from patient learning of clinical trials outside the clinic, and possible selection bias from convenience sample. This study is also only generalizable to patients in care, the poor, symptomatic, and urban.

A later study by Sengupta and colleagues test institutional distrust as the primary factor affecting research participation using a multidimensional construct.<sup>37</sup> They found distrust to be the strongest inverse predictor of willingness to participate in clinical research among 301 African Americans in Durham, NC. Other factors significantly associated with participation were altruism, facilitators/barriers, religiosity, and economic group membership. Of importance to this discussion, over half of the facilitators/barriers construct was accounted for by issues of transportation and number of visits to the study site. Although this study appears to be of good internal validity, this author needs further instruction to determine its true quality. In addition, the results may not be widely generalizable.

The best evidence for barriers to HIV trial participation, however, is likely a recent systematic review by Mills and colleagues (Table 15).<sup>55</sup> Its strong internal validity involves extensive search techniques, concrete selection and grading criteria, and reliable analysis techniques. Furthermore, two of the five qualitative studies and six of the nine quantitative studies analyzed have equitable or near-equitable enrollment of black and white Americans, lending great strength to the external validity.

Three of the five qualitative studies identified themes regarding safety, pragmatic obstacles, and discrimination/social issues. Four of these studies identified fear or

mistrust as a barrier, while all five identified concerns about research design as a barrier. For the barriers identified among the quantitative data:

- Three studies identified discrimination as a barrier to research participation.
- Five studies identified safety as a barrier.
- Six studies identified concerns about research design as a barrier.
- Eight studies identified fear or mistrust as a barrier.
- Eight studies identified pragmatic issues as a barrier.

## Objectives

Although there is evidence available regarding barriers to research participation among minorities, and black Americans in particular, this area of research is by no means saturated or all inclusive. In particular, studies investigating minority participation in HIV and AIDS clinical research generally involve urban populations. As seen in North Carolina and others states, however, an increasing proportion of HIV and AIDS cases live in rural areas. Inclusion of rural minorities in HIV/AIDS research may in fact involve obstacles unique to their environment. In short, the barriers to HIV/AIDS research participation among rural African Americans may be different than those in urban or suburban African Americans. The relative importance of certain barriers may also vary for this population as well.

In this investigation, we will use qualitative and quantitative methods to generate as well as test hypotheses about barriers to participation in clinical research among rural African Americans in North Carolina. My objectives are:

- To investigate which characteristics are associated with past research participation among our sample using quantitative methods.
- To outline the methods for a future qualitative analysis of the respondents' interviews.
- To compare the quantitative results with the existing scientific literature.
- To draw conclusions regarding possible solutions to minority non-participation in medical research.

## Methods

### *Recruitment*

Participants were recruited from three NC sites: the Robeson County Health Department (RCHD), the Rocky Mount Opportunities Industrialization Center (OIC), and at the UNC General Clinical Research Center (GCRC) in Chapel Hill. Onsite staff identified potentially eligible participants for inclusion into this sample. Eligible individuals were ethnic minorities living with HIV or AIDS who were 18 years of age or older. 69 individuals with HIV/AIDS were asked to participate, and 47 completed interviews.

### *Data Collection*

Participants were interviewed via a semi-structured interview guide, consisting of open-and close-ended questions. All interviews were audio recorded, transcribed into an electronic text document, and reviewed twice for accuracy and completeness.

### *Questionnaire Design*

Three questionnaires were developed and color coded according to answers from several preliminary questions (see Appendix I & II). These questions separated respondents into those who have previously enrolled in a research study, those who have been asked to participate but have never enrolled, and those who have never been asked. Each questionnaire consisted of open- and close-ended questions. This format allows exploration of patients' underlying motivations, explanations, or feelings about their responses. Each questionnaire queried participants about their experience related to research participation. Data were also collected about HIV/AIDS experiences, and non-identifiable demographic characteristics, which will enable some assessment of possible confounders.

A previously validated scale was adapted to assess participant trust in HIV researchers<sup>56</sup>. The scale consists of 11 items, has a Cronbach alpha of 0.89, and explores four of the five previously conceptualized domains of trust: fidelity, competence, honesty, and global trust. The question regarding the fifth domain, confidentiality, did not correlate well with the overall scale (0.37) and was therefore deleted from the final construct. The absence of this last domain is significant, given the vulnerability of this study population and the focus of our study question. The inclusion of open-ended prompts within the questionnaire/interview, however, is adequate for recording any confidentiality concerns related to research participation.

Questions assessing participant motivation for research participation were adapted from two previously published studies examining this topic in psychiatric and cancer patients, respectively.<sup>57, 58</sup>

### *Quantitative Analysis*

All quantitative data was entered into electronic documents by two persons for verification. Entry ranges and checks were used to minimize errors.

All variables were examined for normal distribution using means for continuous variables, medians for categorical variables, and histograms when appropriate.

Bivariate analysis was performed using Pearson's Chi-square test or Fisher's Exact test for comparisons of categorical variables. Two-sample t-tests or Wilcoxon Rank Sum were used for comparisons of continuous and categorical variables.

Non-rural housing, race, receipt of public assistance, annual income, educational level, and employment status are the socio-demographic characteristics hypothesized to be associated with past trial participation. Being asked to participate in a clinical trial, transportation, trust in medical researchers, current likelihood of trial participation, expected medical benefit, and not having a better option for obtaining HIV-related care are also hypothesized to be related to past research participation.

#### *Qualitative Analysis Plan*

Using multiple teams of two members, the questionnaires were reviewed to develop coding categories. All responses were categorized according to themes, which were named, described, and recorded. This process continued until no new categories arose and reviewers reached consensus on categorization of responses. Codes and sub-codes were subsequently developed for each category, organized, and applied to the comments within the first twenty six interviews. Coded interviews were then reviewed by another reader to ensure consistency.

For this future portion of my analysis, I will review the previously developed codebook and code the remaining questionnaires, applying labels to relevant themes within the text. This process will be repeated independently by another reader and reviewed with me to ensure consistency. Themes relevant to this analysis will then be tabulated and reviewed in detail for qualitative analysis.

## Results

### Univariate Analyses

#### *Demographics*

Forty seven individuals were verbally consented for completion of this study. They were recruited from three study sites at similar distributions. 74.5% of respondents were Black and 87.2% lived in non-urban areas. Males comprised 55.3% of the sample and mean age was 42.4. Respondents reported having completed less than 12 years, 12 years, and more than 12 years of education at 25.5%, 36.2%, and 38.3%, respectively (Table I).

Annual income of less than \$5000, \$5000 - \$20,000, and greater than \$20,000 were reported by 34.0%, 42.6%, and 23.4%, respectively. 21.3% reported working full time while 57.5% were unable to work and received public assistance. Health insurance status was also reported, with 25.5% having none (Table I).

#### *HIV/AIDS Experiences*

The median days since HIV/AIDS diagnosis was 1825 for this sample. 91.5% were currently on HIV medications. 95.7% thought that HIV meds were “definitely worth taking” (Table I).

#### *Clinical Research Experiences*

Among the 49 respondents, 51.1% had been previously asked to participate in a clinical trial and 40.4% had been previously enrolled in a clinical trial.

#### *Clinical Research Perspectives*

87.2% of our sample reported their current likelihood of trial participation as somewhat or very likely. Transportation was a major barrier for participation in clinical trials among 34.0%. On the trust in clinical research scale, ranging from 11 to 55, the mean score was 42.9. Wanting to help future HIV patients and wanting to be a part of research were reasons for participation among 89.1% and 56.5%, respectively. 37.0% reported persuasion from family. Finally, 84.8% and 43.5% indicated medical benefit for self and no better option for obtaining HIV medications as major reasons, respectively (Table I).

### Bivariate Analyses

#### *Demographics*

Location of the participants' recruitment site was associated with past participation in a clinical trial ( $p < 0.001$ ). Those from the GCRC participated at 100%, compared to 17.7% and 12.5% from the OIC and the RCHD, respectively. The difference in past participation between the GCRC and the OIC ( $p < 0.001$ ) and between the GCRC and the RCHD ( $p < 0.001$ ) were both significant. The difference between the OIC and the RCHD was not statistically significant. Sex,

age, residential description, and race did not have a statistically significant relationship with the outcome (Table II).

#### *Socio-economic Status (SES)*

Annual income, educational level, and insurance type were all associated with past participation in clinical trials. Those with higher incomes had a greater history of past trial participation than those with lower incomes ( $p=0.025$ ). When examined by pairs, only the difference between those with less than 12 years of education and those with more than 12 years of education was significant ( $p=0.015$ ) (Table II).

Respondents with higher educational levels also participated more than those with lower educational levels ( $p<0.001$ ). There was no significant difference between those with less than 12 years of education and those with 12 years of education (0.370). The difference between those with less than 12 and more than 12 years ( $p<0.001$ ), as well as between those with 12 vs. more than 12 years ( $p=0.002$ ), were both significant.

The association between past participation and insurance type was statistically significant ( $p=0.028$ ). When examining differences by pairs, only that between private insurance and Medicaid was significant ( $p=0.008$ ).

Receipt of public assistance, full time employment, and inability to work were not associated with past participation.

#### *HIV/AIDS Experiences*

Time since HIV/AIDS diagnosis was significantly associated with past trial participation. Those who have not participated in clinical trials have known of their diagnosis more than three times as long as those who have participated ( $p=0.006$ ). In addition, predictions based on this association reveal past trial participation to decrease as the length of diagnosis increases ( $p=0.015$ ). Currently being on HIV medications and perceptions of the medications' worth were not associated with past trial participation (Table II).

#### *Clinical Research Experiences*

Respondents who have been asked to participate in a clinical trial have a greater history of past participation than those who have never been asked ( $p<0.001$ ).

#### *Clinical Research Perspectives*

Available transportation and trust in clinical researchers were not associated with past participation. Current likelihood of participating in clinical research was also not associated with past participation (Table II).

Among possible reasons for participating in clinical trials, family persuasion ( $p=0.013$ ) and having no better option for obtaining HIV therapy ( $p=0.010$ ) were

associated with past trial participation. Wanting to help future HIV patients, possibility of medical benefit, and wanting to be a part of research were not significantly associated with past trial participation.



**Table I. Respondent Characteristics**

<b>Characteristics N=47</b>	<b>n (%) or Mean (s.d.)</b>	<b>Median</b>	<b>Range</b>
<b>Demographics</b>			
<b>Sex</b>			
Male	26 (55.3%)	--	--
Female	21 (44.7%)	--	--
<b>Age</b>	42.4 (9.8)	41.0	28-78
<b>Location</b>			
GCRC	14 (29.8%)	--	--
OIC	17 (36.2%)	--	--
RCHD	16 (34.0%)	--	--
<b>Residential Description</b>			
Nonurban	41 (87.2%)	--	--
Urban	6 (12.8%)	--	--
<b>Race</b>			
Non-Black	12 (25.5%)	--	--
Black non-Hispanic	35 (74.5%)	--	--
<b>Socio-economic Status</b>			
<b>Receiving Public Assistance</b>			
Yes	27 (57.5%)	--	--
No	20 (42.6%)	--	--
<b>Annual Income</b>			
<\$5,000	16 (34.0%)	--	--
\$5,000 - \$20,000	20 (42.6%)	--	--
> \$20,000	11 (23.4%)	--	--
<b>Education Completed</b>			
< 12 years	12 (25.5%)	--	--
12 years	17 (36.2%)	--	--
> 12 years	18 (38.3%)	--	--
<b>Insurance</b>			
Private	8 (17.0%)	--	--
Medicare	8 (17.0%)	--	--
Medicaid	18 (38.3%)	--	--
Other	1 (2.1%)	--	--
None	12 (25.5%)	--	--
<b>Employment</b>			
Full Time Employed			
Yes	10 (21.3%)	--	--
No	37 (78.7%)	--	--
Unable to Work			
Yes	27 (57.5%)	--	--
No	20 (42.5%)	--	--
<b>HIV/AIDS Experiences</b>			

Reported Days Since Diagnosis	2388.8 (1878.1)	1825	61-7300
Currently on Medications	43 (91.5%)	--	--
Report HIV Meds Definitely Worth Taking	45 (95.7%)	--	--
<b>Clinical Trial Experiences</b>			
<b>Previously Asked to be in Clinical Trial</b>			
Yes	24 (51.1%)	--	--
No	23 (48.9%)	--	--
<b>Previously Enrolled in a Clinical Trial</b>			
Yes	19 (40.4%)	--	--
No	28 (59.6%)	--	--
<b>Clinical Research Perspectives</b>			
<b>Trust Scale (11-55)</b>	42.9 (5.9)	44.0	27-54
<b>Transportation</b>			
"Big Problem"	16 (34.0%)	--	--
"Somewhat of a problem or not a problem"	31 (66.0%)	--	--
<b>Likelihood of Trial Participation</b>			
Somewhat or Very Likely	41 (87.2%)	--	--
Somewhat or Very Unlikely	6 (12.8%)	--	--
<b>Major Reasons for Participating in Trials (n=46)</b>			
Wanting to help future HIV patients	41 (89.1%)	--	--
Possibility of medical benefit for self	39 (84.8%)	--	--
Family Persuasion to Participate	17 (37.0%)	--	--
Wanting to be a part of research	26 (56.5%)	--	--
No better option for receiving HIV Tx	20 (43.5%)	--	--

## Abbreviations:

GCRC – UNC General Clinical Research Center

OIC – Rocky Mount Opportunities Industrialization Center

RCHD – Robeson County Health Department

**Table II. Bivariate Associations Between Past Trial Participation and Respondent Characteristics.\***

Characteristics	Previously Enrolled in a Clinical Trial n=19 (40.4%)	p value	Total N=47 (100.0%)
<b>Demographics</b>			
<b>Sex</b>			
Male	12 (46.2%)	0.373	26 (55.3%)
Female	7 (33.3%)		21 (44.7%)
<b>Mean Age (S.D.)</b>	40.9 (8.9)	0.395	42.4 (9.8)
Predictions for Age		0.391	
20	55.1		
30	47.8		
40	40.6		
50	33.8		
60	27.6		
<b>Location</b>		<0.001	
GCRC	100.0%		14 (29.8%)
OIC	17.7%		17 (36.2%)
RCHD	12.5%		16 (34.0%)
<b>Residential Description<sup>†</sup></b>		0.204	
Non-urban	15 (36.6%)		41 (87.2%)
Urban	4 (66.7%)		6 (12.8%)
<b>Race<sup>†</sup></b>		0.737	
non-Black	4 (33.3%)		12 (25.5%)
Black non-Hispanic	15 (42.9%)		35 (74.5%)
<b>Socio-economic Status</b>			
<b>Receiving Public Assistance</b>			
Yes	8 (29.6%)	0.080	27 (57.5%)
No	11 (55.0%)		20 (42.5%)
<b>Annual Income<sup>†</sup></b>		0.025	
<\$5,000	3 (18.8%)		16 (34.0%)
\$5,000 - <\$20,000	8 (40.0%)		20 (42.6%)
≥\$20,000	8 (72.7%)		11 (23.4%)
<b>Employment</b>			
Full Time Employed <sup>†</sup>		0.066	
Yes	7 (70.0%)		10 (21.3%)
No	12 (32.4%)		37 (78.7%)
Unable to Work		0.080	
Yes	8 (29.6%)		27 (57.5%)

No	11 (55.0%)		20 (42.5%)
<b>Education<sup>†</sup></b>			
<12 years	1 (8.3%)	<0.001	12 (25.5%)
12 years	4 (23.5%)		17 (36.2%)
>12 years	14 (77.8%)		18 (38.3%)
<b>Insurance<sup>†</sup></b>			
Private	6 (75.0%)	0.028	8 (17.0%)
Medicare	4 (50.0%)		8 (17.0%)
Medicaid	3 (16.7%)		18 (38.3%)
Other	1 (100%)		1 (2.1%)
None	5 (41.7%)		12 (25.5%)
<b>HIV/AIDS Experiences</b>			
<b>Time Since Diagnosis<sup>†</sup></b>			
Median Days (95% CI)	912.5 (429.0-2460.9)	0.006	1825 (1095.0-3089.4)
Predictions for Years		0.015	
0 years	67.7		
5 years	40.8		
10 years	18.4		
15 years	6.9		
20 years	2.4		
<b>Currently on Medications<sup>†</sup></b>			
Yes	18 (41.9%)	0.638	43 (91.5%)
No	1 (25.0%)		
<b>HIV Meds are:<sup>†</sup></b>			
Definitely Worth Taking	19 (42.2%)	0.508	45 (95.7%)
Not Definitely Worth Taking	0 (0.0%)		2 (4.3%)
<b>Clinical Trials Experience</b>			
<b>Previously Asked to be in Clinical Trial</b>			
Yes	79.2%	<0.001	24 (51.1%)
No	0.0%		23 (48.9%)
<b>Clinical Research Perspectives</b>			
<b>Mean Trust Score (S.D.)</b>	43.9 (4.3)	0.335	42.9 (5.9)
Predictions for Trust Score		0.330	
11	11.3		
22	18.4		
33	28.6		

44 55	41.6 55.9		
<b>Transportation</b> “Big Problem”	5 (31.3%)	0.357	16 (34.0%)
“Somewhat or No Problem”	14 (45.2%)		31 (66.0%)
<b>Current Likelihood of Trial Participation<sup>†</sup></b>			
Somewhat or Very Likely	19 (46.3%)	0.068	41 (87.2%)
Somewhat or Very Unlikely	0 (0.0%)		6 (12.8%)
<b>Major Reason for Participating in Trial?</b>			
Wanting to help future HIV patients <sup>†</sup>			
Yes	18 (43.9%)	0.387	41 (89.1%)
No	1 (20.0%)		5 (10.9%)
Possibility of medical benefit for self <sup>‡</sup>			
Yes	16 (41.0%)	1.000	39 (84.8%)
No	3 (42.9%)		7 (15.2%)
Family Persuasion to Participate			
Yes	3 (17.7%)	0.013	17 (37.0%)
No	16 (55.2%)		29 (63.0%)
Wanting to be a part of Research			
Yes	12 (46.2%)	0.446	26 (56.5%)
No	7 (35.0%)		20 (43.5%)
No better option for receiving HIV Tx			
Yes	4 (20.0%)	0.010	20 (43.5%)
No	15 (57.7%)		26 (52.5%)

\*All significance tests for comparisons based on Pearson’s Chi Square for categorical variables and 2-sample t-test for continuous variables unless otherwise specified.

<sup>†</sup>Significance test based upon Fisher’s Exact Test.

<sup>‡</sup>Significance test based upon Wilcoxon Rank Sum.

Abbreviations:

GCRC – UNC General Clinical Research Center

OIC – Rocky Mount Opportunities Industrialization Center

RCHD – Robeson County Health Department

## Discussion

### Interpretation of Results

This study was meant to measure past clinical research participation among minority populations in North Carolina. North Carolina represents a novel setting for such research because of its large rural population and geographic proximity to historical injustices acted out according to race. The rural landscape is thought to impose unique barriers to healthcare acquisition and clinical research utilization. The Southern U.S. legacy of slavery, Jim Crow practices, and segregation may also exacerbate these issues among ethnic groups such as African Americans, Hispanics, and Native Americans.

### Univariate Findings

The sample utilized for this study is thought to provide reasonable representation of the individuals of greatest interest for our questions. Nearly three-fourths of our sample self-identified as Black. Nearly ninety percent did not live in an urban community. In addition, an unfortunately large proportion of participants denied working full-time or being able to work. Participants were heterogeneous regarding sex and age. They were also unexpectedly diverse regarding markers of socio-economic status, such as education or income. This last observation, which will be discussed later, may have significant effects on the bivariate associations and external validity.

Our sample was recruited from three different sites at approximately equal distributions. Bias of results from individual sites is less likely, but overall characteristics of the three recruitment sites may influence the results through selection bias. This will be elaborated upon later.

Concerning HIV/AIDS, the respondents reported high levels of medical care. They also reported rather uniform perspectives of HIV/AIDS medical care. These observations may reflect a certain degree of trust in the medical community. They may also reflect more wide-spread understanding of the importance of HIV care in their disease progression. If the above are true, they may influence the results and also affect external validity. There was wide variation regarding duration of HIV diagnosis, but most respondents reported 12 or fewer years.

This sample reports diverse past clinical research experiences. This suggests that overall bivariate associations are less likely to be biased by respondents' experiences in past clinical research. There are some observations, however, that may be closely associated with past research experiences. Our small sample size precludes precise or accurate analysis of these relationships or statistical adjustments for them. It does, however, permit cautious inference and hypothesis generation for future, more well-powered analyses.

Several variables were recorded to assess perspectives about clinical research. Some of these, such as perceiving transportation as a barrier, show wide variation in responses. This variation may in part be explained by associations with one or several characteristics. Multivariate associations, though not explored for this small sample, cannot be dismissed as unimportant in explaining these variations.

Clinical research perspectives displaying less variation, such as the desire to help future HIV patients, may be more representative of this population as a whole. The small sample size and limited geographic distribution of our participants does not permit wide-spread generalization, however. In spite of this limitation, the characteristics with relatively homogenous responses may suggest local, and perhaps regional, perspectives that are more commonplace than those characteristics with more profound variation.

## Bivariate Findings

### *Demographics*

Among demographic characteristics, only recruitment site was significantly associated with past research participation. This is plausible and expected given the characteristics of the recruitment sites. In particular, the GCRC's chief purpose is conducting clinical research. Thus, participants from this site would be expected to have a higher rate of past research experience than those from the other two sites.

The significant association of recruitment site and the outcome introduces strong intraclass correlation into our analyses. While this is discussed in detail when addressing the appropriateness of our study design, it is important to note that adjustments were not made for the intraclass correlation in these analyses. Calculation of robust standard errors or estimation of multivariate analyses was not possible with three clusters and 47 participants. Stratification by recruitment site would have also rendered most, if not all, of the bivariate associations non-significant. This latter option would also add little to our interpretations.

The most important consequence of intraclass correlation involves inflation of the type I error. Thus, a significance of 0.05 may in fact represent a much higher probability of a falsely significant association. Therefore, caution should be emphasized in all interpretations of bivariate results. Exact p values were reported to facilitate cautious reasoning.

Lack of significant association of past research participation with sex and age were not expected. This investigator thinks that differences in respondent sex or age could have plausible effects on one's decision to participate in clinical research. Younger individuals could conceivably perceive fewer barriers, such as trust, to research participation. Roles and responsibilities that differ by sex could also affect decisions to participate in research. The small differences seen in this sample may in fact be larger and/or achieve statistical significance among larger,



more representative samples. Alternately, common perceptions of clinical research in this sample may be widespread enough to override differences of sex or age.

There was very little diversity among our sample regarding residence in a rural community and race. Therefore, these variables were not expected to have sufficient variation to demonstrate meaningful differences in the outcome. Had our sample represented more diverse race and rural characteristics, however, it is very plausible that past participation would have significantly varied by these characteristics.

#### *Socio-economic Status (SES)*

Education, annual income, and insurance type were significantly associated with clinical research participation. These are plausible and reflect observations seen in other published studies. There were also meaningful differences in past trial participation according to receipt of public aid, full time employment, and inability to work. Their non-significance may reflect a weaker association with the outcome, but this difference may also show statistical significance in larger samples. These markers of SES, however, all reflect a consistent pattern. Those of higher SES have higher rates of past participation. It is possible that these associations are not reflections of differences in intelligence or altruism, but instead reflect greater exposure, access to, and trust in health care and health care professionals. Higher achievement may also favor an increase in inter-ethnic relationships, which may mitigate some amount of the distrust commonly seen in minority populations.

Although the patterns seen for the SES characteristics appear consistent, it is important to note that theoretically, respondents may have felt pressure to report higher markers of SES. This would bias an association between SES and past trial participation away from the null hypothesis. More objective sources for these measurements, such as tax records, would make this bias less likely. Despite this possibility, my suspicion for this bias is low.

#### *HIV/AIDS Experiences*

Length of time since HIV diagnosis was significantly associated with the outcome. This was not an expected association, but it does seem plausible. Those diagnosed in the more distant past may have had vastly different HIV/AIDS experiences than those more recently diagnosed. Differences in such experiences could cause those more remotely diagnosed to be more reluctant to participate in clinical research.

Large differences in past trial participation were also seen according to whether one was currently on HIV medications and whether HIV medications were considered worth taking. These differences were not statistically significant, but are clinically important and may have been significant in a larger sample. These characteristics may actually serve as proxies for trust in the healthcare field,

specific providers, or research personnel. Adjustment for these characteristics, however, may have mitigated this association.

It is also possible that respondents reported certain answers, such as HIV medications being not worth taking, less often because they were socially undesirable. This would certainly bias the results away from our null hypothesis. Since this can not be ruled out with any certainty, recognition of this possibility is important when drawing conclusions.

#### *Clinical Research Experiences*

Positive report of having been asked to participate in clinical research is significantly associated with past participation in clinical research. Aside from the intuitiveness of this association, it may additionally confound many of our associations. Those who have been asked may be very different from those who have never been asked. If so, then the validity of including both groups in this sample may be limited. Future analyses should focus on exploring the heterogeneity of these two groups. Findings may further inform us about trial participation patterns among minority populations.

#### *Clinical Research Perspectives*

Trust in clinical researchers was not significantly associated with past participation. Higher trust scores do appear, however, to reflect higher past research participation. Lack of a significant association is in conflict with our hypothesis and current scientific literature. The predicted difference in trust according to past research participation was sizable and may have achieved statistical significance in a larger sample.

The equal distribution of socio-economic status (annual income and education) among our sample may account for the higher values of trust seen in our sample. Inclusion of more highly educated individuals than is representative of the source population could bias the trust scores upward across both past research participation strata. Respondents may have also been less willing to report socially undesirable responses, such as low trust. Verification of this result in larger samples of rural minorities is needed to further clarify the presence of an association. Such future analyses should also be sufficiently powered to adjust for SES.

Family persuasion to participate in clinical research was significantly associated with having participated in clinical research. Those for whom family persuasion was a major reason reported past participation far less than those for whom it was not a major reason. This result was unexpected, but may reflect a concern for confidentiality in research participation. If all had equal confidentiality concerns, the difference in their past trial participation may in fact lessen or disappear.

Those for whom “not having a better option for obtaining HIV medications than to participate in clinical research” was a major reason for research participation

were predicted to have participated significantly less than those for whom it wasn't a major reason. Those who report it as a major reason, however, may in fact have less trust and be less well connected with the health care field. Accounting for these factors may eliminate this difference. Alternately, some respondents may have been unwilling to report this as a major reason to avoid social discomfort. If so, their responses would bias the results away from the null hypothesis and therefore account for the difference seen.

Meaningful differences in past trial participation that were not statistically significant were reported for perception of transportation as a barrier to participation, current likelihood of research participation, wanting to help future HIV patients, and wanting to be a part of research. Larger sample sizes may actually show statistically significant differences for all of these associations. Perception of transportation and current likelihood of participation may also be confounded by SES and trust, respectively.

The possibility of medical benefit for self as a major reason for research participation showed very little variation according to past participation. A more well-powered study will likely not change this result. Interpreting this non-significant association as is suggests that it is not an important factor in this sample. This result may, however, represent social aversion to reporting this motive, which could bias results towards the null hypothesis or even in an opposite direction—those reporting no having higher participation rates.

## Discussion of Results in Regard to the Existing Scientific Literature

Although there are many scientific papers which discuss barriers and/or facilitators to clinical research participation, very few examine past or current willingness to participate as an outcome. Seven papers that fulfill this criterion will be referenced in regards to comparisons with our results.<sup>49, 51, 52, 54, 59-62</sup>

### *Demographics*

Recruitment site was the only demographic variable significantly associated with past trial participation in this sample. This was expected because of the different characteristics the three sites. Specifically, the UNC General Clinical Research Center is expected to have a patient population with much more experience regarding clinical research than the average outpatient clinic. Similar associations have been reported in two cross-sectional studies (Table 14).<sup>54, 63</sup> Advani and colleagues found willingness to participate in a clinical trial to be dependent upon clinic site. Stone and colleagues do not explicitly report an association between clinic site and participation, but they do adjust for clinic type in their multivariate analyses. Both suggest that characteristics of study or recruitment sites may be related to the outcome and potentially bias other associations. When planning small studies or using only a few recruitment sites, the choice of these sites is even more important. The ability to control or adjust for site characteristics may be limited or impractical in these situations.

Age was not statistically associated with past research participation, but does appear to increase with nonparticipation in this sample. Shavers and colleagues and Tello and colleagues both present findings that mirror this finding (Table 12)(Table 16).<sup>51, 52, 62</sup> Corbie-Smith and colleagues, however, report a similar non-significant age association among black women, but a significant association between age and participation among white women and black and white women combined (Table 17).<sup>49</sup> These suggest that greater age may be a deterrent to research participation, but perhaps more so for whites than blacks. The smaller sample of black women may have also limited power to detect a difference. Other studies among racially diverse samples similarly show greater age as a deterrent to research participation (Table 18).<sup>61, 63</sup> Our results suggest a similar pattern, but this analysis may lack the statistical power to detect a difference among so few participants. Age may also be less of a deterrent for black populations than more ethnically diverse populations.

For this study, racial/ethnic group was not related to past clinical research participation. This is in contrast to much of the existing literature, but is expected given the racial homogeneity of our sample. Several studies have shown blacks to be less willing to participate in research than whites (Table 14)(Table 18).<sup>54, 61, 63</sup> In addition, blacks appear to differ from whites regarding their characteristics associated with participating—or not participating (Table 12)(Table 17)(Table 19).<sup>49, 51, 60</sup> For example, blacks' participation in research may be more associated with joining HIV vaccine trials to reduce their HIV risk behavior and for personal

benefits such as free HIV testing, counseling, financial reimbursement, medical care, or current information on HIV, than white participants.<sup>60</sup> Thus, our non-significant result regarding race and past research participation is a reflection of the study design more so than actual respondent characteristics or responses.

Sex was also not a significant predictor of past research participation in our pilot data, but does show more men participating than women. The current literature is conflicting regarding the significance of sex in predicting research participation among African Americans. Shavers and colleagues report no significant overall association between sex and willingness to participate in a medical research study (Table 12).<sup>51, 52</sup> This finding remained non-significant when stratified by race, but the lower willingness of males among white respondents appears clinically relevant and approaches a significant alpha level ( $p=0.09$ ). Tello and colleagues also nonsignificantly report men as less willing to participate (Table 16).<sup>62</sup> In contrast, Stone and colleagues report women as significantly less likely to participate than men in a sample of ~40% blacks and ~30% whites (Table 14).<sup>54</sup> This difference was not significant when adjusted for age, education, and clinic type. The higher educational level of Shavers' sample may account in part for her statistically non-significant result.

Despite this scientific uncertainty, it is historically well known that women have been under-represented in clinical research. Furthermore, women may have different reasons for choosing to participate in clinical research. Colfax and colleagues reported women to be significantly more likely to participate in an HIV vaccine trial for protection, to reduce high risk behavior, and for composite personal benefits, such as free HIV testing, counseling, and financial reimbursement (Table 19).<sup>60</sup> Women's differing societal status as compared to men provides ample opportunity for differences in research participation behaviors. These societal differences may have important effects on research participation, which may also be associated with the type of research, the environment, and the risks involved.

Urban or non-urban residence was also not statistically associated with past research participation, but does display a clinically important difference. Urban individuals appear to have participated nearly twice as much as non-urban residents. This was expected given that rural communities may have fewer research resources than urban communities.<sup>64</sup> In addition, physicians practicing in rural areas may be less likely to know of clinical research opportunities or to provide such support through their practice. The burden of seeking these services can result in reduced income from lost work, lost time, and costs associated with travel. I was unable to find articles examining an association between rural or urban residence and research participation. I believe, however, that the lack of a significant association in this data analysis is due in part to limited statistical power and few urban residents in our sample. This clinically relevant difference according to urban residence should be followed up in a larger sample to further explore this possible association.

### *Socio-economic Status*

Markers of socio-economic status (SES) are consistently associated with research participation in the scientific literature. Of annual income, receipt of public assistance, employment status, educational level, and insurance type, only annual income, education, and insurance type were statistically significant in this pilot study.

Education is consistently reported in several studies as associated with clinical research participation (Table 12)(Table 18).<sup>51, 59, 61</sup> In these references, higher education is associated with a higher likelihood of research participation. This pattern persists for Shavers & colleagues' work when stratified by race, but does not remain significant for blacks. This may be because of the few numbers of respondents in the lowest educational categories for this study. Higher education appears related to higher participation rates among 97 black women in the work of Corbie-Smith and colleagues also, but is similarly non-significant (Table 17).<sup>49</sup> Given the low alpha level reported for our educational association and the trends seen in the current literature, higher education is likely a significant predictor of research participation.

Income appears less commonly reported as an SES variable for our relevant studies, but Advani does report it as significantly associated with participation.<sup>59</sup> Shavers, however, does not report a significant association for her overall sample or when stratified by race. It is likely that income does predict research participation, but not as well as educational level. Educational level may approach the underlying concepts or themes of SES more closely than income.

There were no available studies with which to compare our results regarding insurance type, receipt of public assistance, or employment status. Similar to income, however, these variables all likely provide at least some predictive value for research participation, but perhaps not as well as education.

A more appropriate question given these findings is why higher SES is associated with increased clinical trial participation? It is likely that those of higher SES may be more equipped to overcome, or are less vulnerable to, social, cultural, regional, and economic barriers regarding the health care system. Specific reasons or motivations for research participation may also vary according to SES and likely play some role in the decision making process. For example, Colfax reports that those with higher educational levels may be less likely to participate in an HIV vaccine trial to reduce their risk behaviors or for personal benefits.<sup>60</sup> Differences such as these may further illuminate how to overcome minority under-representation in medical research.

### *HIV/AIDS Experiences*

There are few available articles that address HIV/AIDS experiences and their possible association with research participation. Stone and colleagues report progression to AIDS as significantly associated with research participation (Table

14).<sup>54</sup> CD4 count  $\leq 200$  also seemed associated with increased participation, but was not statistically significant. Those ever tested for HIV-1 were significantly more willing to participate in a vaccine trial in a study published by Tello and colleagues (Table 16).<sup>62</sup> The characteristics measured in this sample, such as the time since diagnosis, being currently on medications, and reporting HIV medications as worth taking, can be seen as proxies for HIV severity. In this light, being currently on medications and considering them worthwhile agree with Stone's findings, while length of time since diagnosis does not. This last disagreement may be a reflection of younger age in those more recently diagnosed or a generational change in other characteristics, such as trust—the more recently diagnosed may have more trust.

These variables may also be viewed, however, as proxies for trust or comfort with the health care system. Those who were recently diagnosed, who consider their medications worth taking, or who are on medications may interact with the medical system better or differently than their counterparts. This latter perspective appears synergistic with that of disease severity—its relationship to past research participation is similar. As such, the relative contribution of each perspective to our results cannot be teased out. Fortunately, more specific questions were asked regarding trust. In short, more recent diagnosis, currently taking HIV medications, and considering HIV medications as worth taking appear to reflect high participation rates.

#### *Clinical Trials Experience*

Individuals' experiences regarding clinical trials can have important implications on their subsequent participation. For this study, only past invitation to participate and past participation itself were measured. These two were very strongly related. There were no articles to compare this to, but Advani and colleagues do compare invitation to participate in research according to race.<sup>59</sup> They saw no difference between African Americans and Whites.

Research experiences may also include knowledge about clinical research. Two cross-sectional studies which assess respondents' knowledge report interesting associations. Shavers and colleagues report that knowledge of the Tuskegee Syphilis Study was not associated with research participation (Table 12).<sup>51</sup> The effect of that knowledge on trust in medical researchers, however, was related to willingness to participate in medical research. Those who lost trust in researchers were much less likely to participate than those with unchanged or increased trust in medical researchers. This is an example where the knowledge appears to not be important.

In another cross-sectional study, Advani reports that those with knowledge of clinical trials as "experiments" on people and knowledge of research participants as "guinea pigs" were significantly less likely to participate in medical research.<sup>59</sup> Alternatively, positive knowledge about research, such as the collection of more information on a therapy, possible societal or personal benefit, or simply knowing

someone else who has participated, was significantly associated with increased willingness to participate. This example highlights the importance of knowledge as part of the respondents' experiences.

The significant association of clinical trial experience with willingness to participate in clinical research can cause difficulty in drawing conclusions in cross-sectional studies. Without follow-up, one can not know if the factor of interest is causal or whether past or current experiences, such as those pertaining to clinical trials, are causing the association. Recognizing this may lead to new research questions. In reference to this data set, the difference (if any) between those who have and have not been invited to participate in medical research is of particular interest.

#### *Clinical Research Perspectives*

Although many variables were measured for respondents' perspectives regarding clinical research, only family persuasion to participate and not having a better option for obtaining HIV therapy were statistically associated with past research participation. Trust in medical researchers, transportation as a barrier to participation, current likelihood of trial participation, wanting to help future HIV patients, and wanting to be a part of research also show patterns suggestive of a relationship, however.

Although not significant, those with higher trust scores appear more willing to participate in research in our sample. Lower measures of trust have been previously associated with African American ethnicity, but have not been studied in relation to willingness to participate as comprehensively (Table 13).<sup>53</sup> As mentioned previously, Shavers and colleagues reported that decreases in trust resulting from knowledge of the Tuskegee Syphilis study were significantly predictive for non-willingness to participate in medical research (Table 12).<sup>51</sup>

Buchbinder and colleagues also report African Americans as citing mistrust of government and drug companies as reasons for refusing participation much more often than Whites, though statistical tests were not performed.<sup>61</sup> Stone and colleagues show a non-significant difference in fear of experimentation—a proxy for trust—between persons of color and whites.<sup>54</sup> The pattern seen in our results and the literature suggests that trust is associated with willingness to participate in medical research. This association needs to be tested in a larger study, however, to prove its validity.

Transportation is a conceptually expected barrier to research participation among rural populations. Few quantitative studies, however, have assessed this. Our results show that those denying transportation as a problem participated more often. Both Advani and Buchbinder report similar, but statistically non-significant, findings (Table 12)(Table 18).<sup>51, 59, 61</sup> Although transportation is likely an important determinant in rural populations, confirmation in a larger sample is necessary for definitive conclusion drawing.



Current willingness to participate appears positively correlated with past research participation in our results. Buchbinder similarly reports that those with past willingness to participate enrolled in their study at higher rates than those less willing in the past ( $p < 0.001$ ) (Table 18).<sup>61</sup> Although both associations seem valid, repetition in a larger study is definitely warranted. In addition, it is noteworthy that past willingness is not a great tool for use in recruitment. Both our results and, more appropriately, Buchbinder's results, show that relatively small percentages of those who indicated past willingness actually participated at the time of enrollment.

Despite statistical non-significance, several reasons for participating research appear related to past participation in studies. In our results, wanting to help others with HIV and expecting medical benefit for self appeared related and unrelated to past participation, respectively. These are supported by papers by Advani, Shavers, and Colfax (Table 12)(Table 19).<sup>52, 59, 60</sup> Our results concerning family influence on decision to participate appears similar to those presented by Advani.<sup>59</sup> Wanting to be a part of research was not assessed in any of the available literature.

Lastly, those for which not having a better option for obtaining HIV therapy was not a major reason for participating in research participated more than those for whom this was a major reason. None of the available studies compared these two characteristics. Several did, however, report how significant of a facilitator this was for participating. Shavers and Advani report it as a very important factor among their samples (Table 12).<sup>52, 59</sup> Colfax and colleagues, however, report that < 10% of men and < 30% of women in their sample agreed that receipt of medical care was an important motivator for their research participation. The overall high risk for HIV within this latter sample, however, may account for this difference in motivation.

## Discussion of Analysis Plan

### *Choice of Outcome Measure*

Choosing an outcome for this data analysis proved very difficult. The two most compelling options for an outcome were past clinical trial participation and current willingness to participate in a clinical trial.

Past trial participation was measured in all respondents via the structured interview. It was recorded as a binary variable, "yes" or "no." Of those who responded no, many had also never been asked to participate. The past trial participation variable may therefore actually represent three possible responses: Never asked, asked but not enrolled, and enrolled. The former two categories were condensed into the "no" response, however, for practical purposes. Such a small sample may not have had adequate power to discern between three outcome categories. Investigating the role of being previously asked to participate would be better served in the context of a larger sample size.

Current willingness to participate in a clinical trial was measured in those who had never enrolled in a clinical trial. Use of this variable for the outcome would have required

restricting the sample to the 28 who were asked, assuming that the remainder of the sample are currently somewhat or very likely to participate, allocating responses to the 19 via some previous estimate of willingness, or randomly allocating responses for the 19.

Past trial participation was a better choice firstly because all participants were asked this question, as compared to current willingness. For current willingness, restricting to only 28 respondents would have compromised statistical power. Alternately, assuming current willingness for the 19 may have artificially inflated the number of cases and ignores possible contributions of past research experiences to their current willingness. This could bias all of the bivariate associations towards or away from the null. The unavailability of estimates for current willingness in those who have previously participated prevented allocation of these responses on objective evidence. Finally, randomly allocating the responses for 40% of the sample may have biased results to the null. This may also ignore the contribution of past clinical trial experiences to current willingness among the 19 individuals. In lieu of compromising statistical power, introducing concerns of confounding, or potentially biasing the results, past participation was chosen for its less profound measurement bias and confounding issues.

Past trial participation is theoretically dependent upon actually being asked to participate. Only 51.1% of this sample had ever been asked. Although whether one was asked to participate in a trial confounds the bivariate relationships, there were several options available to deal with it. Restriction or stratification of the non-past trial enrollees to only those who had been previously asked would reduce the already small sample size and therefore decrease the statistical power

to detect differences in the outcome. Modeling with logistic regression could also account for this covariate. This was precluded, however, by the small number of independent variables allowed in the model. The negative responses to this covariate also predict the outcome perfectly. This latter violates an essential assumption of logistic regression and prevents its use. A final option is simply reporting the unadjusted bivariate associations. This of course requires reporting the relationship of the covariate to the outcome, but recognizing that the sample size is too small to estimate its contribution.

In short, past trial participation was chosen for its completeness, less concern for measurement bias, and its partial, though inadequate, potential for adjustment with restriction or stratification.

### *Analysis Plan*

The quantitative analysis plan used for this secondary data analysis was designed to be exploratory in nature. Exploratory analyses were more appropriate than testing theoretical hypotheses because of the very small sample size. Small samples may not be representative of the larger population. Therefore, any statistically significant results are generalizable only to that sample. For this reason, small samples are generally used for hypothesis generating. Associations or patterns may be used for developing or refining subsequent hypotheses and tested in larger, more representative samples. With this goal, univariate and bivariate analyses were ideal for characterizing this sample.

Statistical power was also a very relevant limitation when constructing the analysis plan. For multivariate analysis, the binary outcome required logistic regression. Previous estimates of one independent variable for each 10 cases of the outcome would have limited models to two independent variables for 19 cases. Two independent variables were adequate to adjust the bivariate results for one potential confounder, but prevented estimation of a larger model.

### *Strengths/Weaknesses*

The statistical methods used for this study are strong and appropriate. The continuous variables were appropriately examined for a normal, linear relationship to the outcome before choosing parametric statistical tests. Non-parametric tests were used when the above was not present or in question. Comparisons of categorical variables used Fisher's Exact test instead of Pearson's Chi Square test when an expected value in any cell was very small ( $< 5$ ). All statistical tests were also two-tailed with a 5% alpha level and 80% power.

This data analysis was, however, limited by its study design. The small sample size firstly limits more detailed analyses of associations within this sample. Estimation of a multivariate model for all characteristics associated with the outcome was not possible. Simultaneously controlling for more than one covariate was also not statistically appropriate.

Secondly, the choice of recruitment sites for this study imposes significant intraclass correlation from upon the results. Large intraclass correlation, as seen in this study, can inflate the alpha level such that falsely concluding a statistically significant result becomes more likely. Furthermore, statistically adjusting for the intraclass correlation was not possible in such a small sample. Although I considered stratifying by site or lowering the significance level, I ultimately chose to simply present the data for what they were—pilot data—and subsequently draw cautious inferences regarding the patterns seen. By reporting the exact p values, I hope to provide the reader with enough information to critically examine my conclusions and make their own inferences.

The results reported for this study have fair potential to be affected by measurement bias. While all parameters were measured and recorded consistently by trained staff, some questions may have been perceived as socially sensitive. If so, then respondents may have felt pressured to report more socially desirable answers, such as higher trust in researchers or not perceiving medical benefit for self as a major reason to participate in research. This is a common, but often unavoidable limitation to social science research.

There may also be fair potential for selection bias in this study. Eligible patients were identified non-randomly and may have been very similar within recruitment site. It is unknown how exactly this might bias our results, but a more non-systematic method of recruitment would have minimized this possibility. The inclusion of more sites may have further mitigated the potential for selection bias.

Given the concerns regarding selection bias, measurement bias, and study design, the internal validity of this study is fair. The weaknesses presented are enough to cause some concern, but not sufficient to consider the entire study invalid. Furthermore, this study has very limited external validity. Generalizations can only be made to the recruitment sites from which the participants came. Their non-random selection and small sample size limit generalizations to larger populations. Even so, the results presented here remain important. They provide important preliminary information regarding clinical research behaviors and outlooks among rural minorities, a population not often studied for HIV/AIDS.

## Conclusions

### *Demographics*

In this analysis of 47 rural minorities, ~40% reported past participation in a medical research study. Among this 40%, males appeared to participate more often than women. There is some support for this association in the literature. This may be a reflection of women's historical exclusion from medical research. There may also be important differences in the reasons for participation between men and women.

Older age appears to be associated with lower participation in research. This is supported by the literature, although age may not be as strong of a predictor among blacks as it is among whites.

Recruitment site was significantly associated with past research participation. Furthermore, recruitment site characteristics are very important when planning a study. When possible, care should be taken that site characteristics are not strongly associated with important outcome or predictor variables. Such associations may be adjusted for in larger studies, but are very troublesome in smaller samples.

Urban participants appeared to enroll in research studies more often than non-urban participants. Though not statistically significant or verified in the literature, this observation does address an original question and provide important clues regarding future analyses and possible results.

Race is an important predictor of willingness to participate in medical research in the scientific literature. These usually involve comparisons of black and white populations. Our sample did not detect a difference between blacks and non-blacks, but also only had one white participant. Therefore, our results suggest little difference in research participation between blacks and other ethnic minorities.

### *Socio-economic Status*

Socio-economic status (SES) is an important predictor of research participation in our study and in the literature. Although several specific variables appeared significant, education may be the strongest predictor among those we measured.

### *HIV/AIDS Experiences*

HIV/AIDS experiences show an association with research involvement, but may be reflective of two underlying themes. Firstly, the sickest may be more likely to enroll in studies than the less sick. The exception here, however, is the respondents' length of time since being diagnosed. Those more recently diagnosed appear to participate more than those diagnosed less recently. This may be because the introduction of HAART has weakened the association

between length of HIV diagnosis and disease severity. Also, the more recently diagnosed may reflect a generational increase in trust regarding medical research.

The second underlying theme is that HIV/AIDS experiences may serve as proxies for trust or comfort with the healthcare system. Our trust scale, however, would likely serve as a much better indicator for this theme than HIV/AIDS experiences. For future analyses, more narrow definition of HIV/AIDS experiences to measure only disease severity may be more useful.

### *Clinical Trials Experiences*

Various clinical trial experiences show associations with research participation in our study, but more so in the literature. These associations are of particular interest because they may confound our other bivariate relationships. Because of their basic relationship to our outcome, questions regarding their role in deciding to participate in clinical research may lead to new and equally important research questions and hypotheses.

### *Clinical Research Perspectives*

Though not statistically significant, the pattern between trust in researchers and past research enrollment in our study parallel the results cited in several scientific publications. Larger sample sizes may be needed, however, to better assess its importance.

Considering transportation as a major barrier to research participation was statistically non-significant when assessed with past research participation. It did, however, show participation to be higher among those who didn't consider transportation to be a barrier. The importance of transportation has not been widely addressed in the literature, as was the case with urban/non-urban residence. These both represent novel findings, however, that are adequate to support future, more well powered investigations into their significance.

Past participation in research relates well to current willingness to do so. Similarly, the literature shows past hypothetical willingness to be associated with "current" decision to enroll in a research study. These both suggest a permanence of perspective over time with regards to willingness. They both also show that past estimates of willingness are imperfect and not to be used for actual recruitment methods.

Non-perception of family persuasion as a major reason and perception of not having a better option for obtaining HIV therapy as a major reason for research participation were both significantly associated with past research enrollment. These were both also supported in the literature. The increased participation among those not considering family persuasion important may reflect a need or desire for confidentiality regarding their HIV and any associated treatments, care, or research participation. Aversion to socially undesirable answers may account

for the high participation rates among those denying using research for obtaining HIV care.

Wanting to help future HIV patients and wanting to be a part of research were not statistically significant in their association with past research participation, but do show meaningful differences. The association with wanting to help future HIV patients is supported in the scientific literature. Denial of the importance of this altruistic motivator, however, may have been under-reported due to social pressures. Wanting to be a part of research was not assessed in the literature, but may similarly be perceived as altruistic and therefore difficult to report as unimportant.

Lastly, medical benefit for self showed no meaningful difference or significant association with past research participation. Similar findings are seen in the scientific literature, but are subject to social pressures. Many respondents may have felt this to be important, but were afraid to report it so.

## Appendix I.

ID: \_\_\_\_\_ Location: \_\_\_\_\_ Time Start: \_\_\_\_\_  
 Date: \_\_\_\_\_

### Persons Living with HIV/AIDS Interview Guide Screening Cover Sheet

**[Read information sheet to respondent or give them time to read it themselves.  
 Leave copy with them]**

We appreciate your time and participation in helping us learn more about persons living with HIV/AIDS. We are interested in learning more about your experiences with clinical research. In an effort to better understand your experiences, this survey will ask questions about your experiences living with HIV/AIDS and your experience with clinical trials in HIV/AIDS research.

**\*\*\*Important: For GCRC Participants, please have them first check in for our protocol, #2186, if they are willing to participate.\*\*\***

Because we ask you a lot of in-depth questions, we like to tape record the interviews so we don't miss anything important that you say. Your name will not be anywhere on the tape. If you want me to stop the tape at any time, you can just let me know. Is it all right to tape the interview?

- ☐<sub>1</sub> Yes  
☐<sub>0</sub> No

**\*\*\*[If Yes, Start Tape Recorder Now]\*\*\***

The following brief screening questions will help me to determine which survey will apply to your experiences while making the best use of your time during this interview.

**[Interviewers will use answers to following questions to determine which color interview guide they will use]**

**S1. Have you ever been asked to be in a clinical trial for HIV/AIDS treatment? By clinical trials we mean research studies that are being done to find out the best combinations of drugs for treatment of HIV.**

- ☐<sub>0</sub> If no, please proceed to the pink survey  
☐<sub>1</sub> If yes, please proceed to question S2.

**S2. Have you ever taken part (enrolled) in any clinical trials?**

- ☐<sub>0</sub> If no, please proceed to the blue survey



☐<sub>1</sub> If yes, please proceed to the **green survey**

## **Appendix II.**

### **Interview Guide for people who did not enroll in clinical trials (Blue Version)**

#### **Clinical Trials**

First we have a few questions about your understanding of clinical trials. By clinical trials we mean research studies that are being done to find out the best combinations of drugs for treatment of HIV.

**1. What have you heard about clinical trials for HIV/AIDS?**

**Probes:**

- a. Have you ever heard of any trials for HIV/AIDS?
- b. What do you think they are?
- c. How would you explain it to someone who had never heard of it?

You told us that you have been asked to participate in at least one clinical trial, but that you did not take part in any trials. For the next several questions, please think about the most recent study you were asked to take part in.

**2. How did you first hear about the study?**

**3. What were your reasons for not taking part?**

**4. What, if anything, would have made it easier to take part in this study?**  
*[Free List]*

**5. What, if anything, were some fears or concerns you had about taking part in the clinical trial? [Free List]**

6. What, if anything, sounded good about this study? *[Free List]*
7. What, if anything, sounded bad about this study? *[Free List]*
8. What would you tell a friend who was considering enrolling in a clinical trial about your experience hearing about this study?

Now we have a few questions about HIV/AIDS clinical trials in general. Remember, by clinical trials we mean research studies that are being done to find out the best combinations of drugs for treatment of HIV.

9. What do you think would make it hard for other people with HIV/AIDS to take part in clinical trials? *[Free List]*
10. What do you think would make it easy for other people with HIV/AIDS to take part in clinical trials? *[Free List]*
11. If you were asked to take part in a clinical trial now, how would you feel about it?

**Probe:** Who would you talk to about being in a trial?

**12. How likely would you be to take part?**

- ☐<sub>1</sub> Very likely  
☐<sub>2</sub> Somewhat likely  
☐<sub>3</sub> Somewhat unlikely  
☐<sub>4</sub> Very unlikely

**13. Probes:**

If “very likely” to Q12: Why would you be very likely to take part?

If “somewhat likely” to Q12: Why would you be somewhat likely to take part?

If “somewhat unlikely” or “very unlikely” to Q12: Why wouldn’t you be likely to take part?

**14. I’m going to read a list of reasons why some people may decide to take part in a clinical trial. As I read each one, please tell me whether each of these would be a major reason, a minor reason, or not a reason you would take part in a clinical trial.**

	Major Reason	Minor Reason	Not a Reason
a. Trust in the doctor who referred you to the trial	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>
b. Trust in the doctor who would be taking care of you in a research trial	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>
c. Trust in the nurses who would be taking care of you in a trial	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>
d. Wanting to help future HIV patients	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>
e. The possibility of medical benefit to you	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>
f. Your family would want you to do it.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>
g. Wanting to be part of research.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>
h. Not having a better option for getting treatment for your HIV.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>

**15. Was there some other important reason not mentioned yet?****16. Do you think you would get medical benefit from taking part in an HIV clinical trial?**

Probe for why/why not

**17. Did you think you would get emotional benefit from taking part in a trial?**

**Probe:** That is, you would have a better emotional outlook

**18. Some people have told us that one reason they haven't taken part in clinical trials at UNC is because they have to travel so far to get there. How much of a problem is that for you? Is that:**

- ☐<sub>1</sub> A big problem
- ☐<sub>2</sub> Somewhat of a problem
- ☐<sub>3</sub> Not a problem at all

**19. If a van were to come out to your community to conduct clinical trials, how would you feel about that?**

**Probe:**

- a. How would you feel about getting on a van for medical services (e.g. drawing blood, getting medication...)?
- b. Clarify if necessary: This will not be a van that is just for HIV/AIDS, it will have other services with it as well, such as blood pressure screening, so that no one would know why anyone was getting on the van.

**20. How likely would you be to take part in a clinical trial study, if a van came right to your neighborhood? (*Read Choices*)**

- ☐<sub>1</sub> Very likely
- ☐<sub>2</sub> Somewhat likely
- ☐<sub>3</sub> Somewhat unlikely
- ☐<sub>4</sub> Very unlikely

**21. Probes:**

If "very likely" to Q20: Why would you be very likely to take part?

If "somewhat likely" to Q20: Why would you be somewhat likely to take part?

If "somewhat unlikely" or "very unlikely" to Q20: Why wouldn't you be likely to take part?

**22. What do you think would be good ways for researchers to tell people about clinical trials?**

**Probes:**

- a. What would be good ways for them to get the word out?
- b. What would be most likely to work with you?

**HIV/AIDS experiences**

Now I am interested in knowing more about you and your experiences in being told you have HIV.

**23. Tell me about when and under what circumstances you were told about your diagnosis?**

**Probe if necessary:** How long ago were you diagnosed?

**24. Tell me what you know about HIV.**

**Probes:**

- a. What it is
- b. How it is spread
- c. How it affects you
- d. How you need to care for yourself when you have HIV

**25. How about AIDS?**

**Probes:**

- a. What it is
- b. How it affects you

**26. In general, what do you know about medications for HIV?**

**Probes:**

- a. Names?
- b. What they do?
- c. How much they cost?
- d. How often you have to take them?

27. Are you presently taking any medications for HIV? ☐<sub>1</sub> Yes ☐<sub>0</sub> No

**Probes:**

- a. type of medication
- b. Frequency of taking
- c. Side effects or other problems
- d. How do they feel about taking this medication

28. Are HIV/AIDS medications (also known as antiretrovirals) worth taking?  
Would you say:

- ☐<sub>1</sub> Definitely
- ☐<sub>2</sub> Probably
- ☐<sub>3</sub> Probably not
- ☐<sub>4</sub> Definitely not

29. Why or why not?

30. Are you presently taking any medications for HIV?

- a. Probe: type of medication
- b. Frequency of taking
- c. Side effects or other problems
- d. How do they feel about taking this medication



**Trust**

Please tell me if you strongly agree, somewhat agree, neither agree nor disagree, somewhat disagree, or strongly disagree with each of the following statements:

	Strongly Agree	Somewhat Agree	Neither agree nor disagree	Somewhat Disagree	Strongly Disagree
31. HIV researchers, in general, care about their study participants' health just as much or more as their participants do.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
32. Sometimes HIV researchers care more about what is convenient for them than about their participants' medical needs.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
33. HIV researchers are extremely thorough and careful.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
34. You completely trust HIV researchers' decisions about which medical treatments are best.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
35. HIV researchers are totally honest in telling their participants about <i>all</i> of the different treatment options available for their conditions.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
36. HIV researchers think only about what is best for their participants.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
37. Sometimes HIV researchers do not pay full attention to what participants are trying to tell them.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
38. HIV researchers always use their very best skill and effort on behalf of their participants.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
39. You have no worries about putting your life in the hands of HIV researchers.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
40. An HIV researcher would never mislead you about anything.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	
41. All in all, you trust HIV researchers completely.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	

**Background**

Now I have a few questions about you:

**Interviewer: DO NOT READ**

42. What is Respondent's sex?

- ☐<sub>1</sub> Male  
☐<sub>2</sub> Female

43. Are you Hispanic/Latino?

- ☐<sub>1</sub> Yes  
☐<sub>0</sub> No

**44. What is your race? (Do NOT read choices, record all that apply.)**

☐<sub>1</sub> Caucasian/White American

☐<sub>2</sub> African American

☐<sub>3</sub> Asian American

☐<sub>4</sub> American Indian or Alaska Native

☐<sub>5</sub> Native Hawaiian/Pacific Islander

☐<sub>6</sub> Other (please specify) \_\_\_\_\_

**45. How old are you?** \_\_\_\_\_

**46. What is the highest grade you completed in school? (Read choices, accept only one response)**

- ☐<sub>1</sub> Less than high school  
☐<sub>2</sub> Some high school  
☐<sub>3</sub> Graduated from high school or GED  
☐<sub>4</sub> Some undergraduate college or technical school  
☐<sub>5</sub> Completed College  
☐<sub>6</sub> Masters Degree  
☐<sub>7</sub> Doctorate Degree

**47. What best describes your employment situation at this time? That is, are you employed full-time, part-time, taking care of home or family, in school, retired, unable to work because of an illness or condition, or something else? (Please check all that apply)**

- ☐<sub>1</sub> Employed part-time  
☐<sub>2</sub> Employed full-time  
☐<sub>3</sub> Taking care of home or family  
☐<sub>4</sub> In school  
☐<sub>5</sub> Retired  
☐<sub>6</sub> Unable to work because of an illness or condition  
☐<sub>7</sub> Something else (Specify) \_\_\_\_\_

**48. What would you say your main occupation is or has been?**

\_\_\_\_\_  
DK  
REF



49. What, if any, kind of health insurance do you have? (*Read Choices*)

- ☐<sub>1</sub> Private
- ☐<sub>2</sub> Medicare
- ☐<sub>3</sub> Medicaid
- ☐<sub>4</sub> Something else, \_\_\_\_\_ (*specify*)
- ☐<sub>5</sub> or None?
- ☐<sub>8</sub> DK (**DO NOT READ**)
- ☐<sub>9</sub> Refused (**DO NOT READ**)

50. Would you describe where you live as:

- ☐<sub>1</sub> Rural
- ☐<sub>2</sub> Urban
- ☐<sub>3</sub> Suburban, or
- ☐<sub>4</sub> Something else? \_\_\_\_\_
- ☐<sub>8</sub> DK (**DO NOT READ**)
- ☐<sub>9</sub> Refused (**DO NOT READ**)

51. What town or city do you live in? (Note to interviewer: If respondent wants to know why we need this, explain it is just so we can figure out how far they have to travel for care).

\_\_\_\_\_

52. Are you getting any public assistance, such as WIC, SSI, Disability, etc?

- ☐<sub>1</sub> Yes
- ☐<sub>0</sub> No

53. Looking at this card (HAND CARD) could you please tell me, before taxes, which one describes your household's total income last year:

- ☐<sub>1</sub> Less than \$5,000
- ☐<sub>2</sub> \$5,000 to less than \$20,000
- ☐<sub>3</sub> \$20,000 to less than \$40,000
- ☐<sub>4</sub> \$40,000 to less than \$60,000
- ☐<sub>5</sub> \$60,000 to less than \$80,000
- ☐<sub>6</sub> \$80,000 or more
- ☐<sub>7</sub> DK/NA [**DO NOT READ**]
- ☐<sub>8</sub> REFUSED [**DO NOT READ**]

Thank you very much for your time. We really appreciate all of the time you gave us and your thoughtful answers.

**\*\*Remember to give cash/food voucher\*\***

**\*\*Interviewers record all observations into tape after interview is over\*\***

Time Ended: \_\_\_\_\_

**Income Categories Card**

- ☐<sub>1</sub> Less than \$5,000
- ☐<sub>2</sub> \$5,000 to less than \$20,000
- ☐<sub>3</sub> \$20,000 to less than \$40,000
- ☐<sub>4</sub> \$40,000 to less than \$60,000
- ☐<sub>5</sub> \$60,000 to less than \$80,000
- ☐<sub>6</sub> \$80,000 or more

## References

1. WHO. *The World Health Report 2000: Health Systems: Improving Performance*. Geneva, Switzerland; 2000.
2. Dean HD, Steele CB, Satcher AJ, Nakashima AK. HIV/AIDS among minority races and ethnicities in the United States, 1999-2003. *J Natl Med Assoc*. Jul 2005;97(7 Suppl):5S-12S.
3. Vu MQ, Steketee RW, Valleroy L, Weinstock H, Karon J, Janssen R. HIV incidence in the United States, 1978-1999. *J Acquir Immune Defic Syndr*. Oct 1 2002;31(2):188-201.
4. O'Brien ME, Richardson-Alston G, Ayoub M, Magnus M, Peterman TA, Kissinger P. Prevalence and correlates of HIV serostatus disclosure. *Sex Transm Dis*. Sep 2003;30(9):731-735.
5. Foundation KF. HIV/AIDS Policy Fact Sheet Fact Sheet]. November 28, 2005; Fact Sheet. Available at: <http://www.kff.org/hiv/aids/upload/3029-06.pdf>. Accessed March 16, 2006, 2006.
6. CDC. Advancing HIV Prevention: New Strategies for a Changing Epidemic -- United States, 2003. *MMWR Morb Mortal Wkly Rep*. April 18, 2003 2003;52(15):329-332.
7. CDC. HIV and AIDS--United States, 1981-2000. *MMWR Morb Mortal Wkly Rep*. Jun 1 2001;50(21):430-434.
8. CDC. Trends in HIV/AIDS Diagnoses --- 33 States, 2001--2004. *MMWR Morb Mortal Wkly Rep*. November 18, 2005 2005;54(45):1149-1153.
9. Harawa NT, Douglas J, McFarland W, et al. Trends in HIV prevalence among public sexually transmitted disease clinic attendees in the Western region of the United States (1989-1999). *J Acquir Immune Defic Syndr*. Sep 1 2004;37(1):1206-1215.
10. Calonge BN, Petersen LR, Miller RS, Marshall G. Human immunodeficiency virus seroprevalence in primary care practices in the United States. *West J Med*. Feb 1993;158(2):148-152.
11. CDC. HIV prevalence estimates and AIDS case projections for the United States: report based upon a workshop. *MMWR Recomm Rep*. Nov 30 1990;39(RR-16):1-31.
12. Bureau USC. Historical National Population Estimates: July 1, 1900 to July 1, 1999. Webpage]. June 28, 2000; Annual U.S. Population Estimates. Available at: <http://www.census.gov/popest/archives/1990s/popclockest.txt>. Accessed March 18, 2006, 2006.
13. Pincus JM, Crosby SS, Losina E, King ER, LaBelle C, Freedberg KA. Acute human immunodeficiency virus infection in patients presenting to an urban urgent care center. *Clin Infect Dis*. Dec 15 2003;37(12):1699-1704.
14. Coco A, Kleinhans E. Prevalence of primary HIV infection in symptomatic ambulatory patients. *Ann Fam Med*. Sep-Oct 2005;3(5):400-404.

15. CDC. Advancing HIV prevention: new strategies for a changing epidemic--United States, 2003. *MMWR Morb Mortal Wkly Rep.* Apr 18 2003;52(15):329-332.
16. Carolina SoN, Services DoHH, Health DoP. *North Carolina Epidemiologic Profile for HIV/STD Prevention & Care Planning* July 2005 2005.
17. Smith DK, Gwinn M, Selik RM, et al. HIV/AIDS among African Americans: progress or progression? *Aids.* Jun 16 2000;14(9):1237-1248.
18. Rosenberg PS, Biggar RJ. Trends in HIV incidence among young adults in the United States. *Jama.* Jun 17 1998;279(23):1894-1899.
19. CDC. *Cases of HIV infection and AIDS in the United States, 2004.* Atlanta 2005 2005. Volume 16.
20. Wong MD, Shapiro MF, Boscardin WJ, Ettner SL. Contribution of major diseases to disparities in mortality. *N Engl J Med.* Nov 14 2002;347(20):1585-1592.
21. Medicine Io. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*; 2002.
22. Valerie E. Stone M, MPH. 2006 Zollicoffer Lecture: Disparities in HIV/AIDS by Race/Ethnicity; 2006.
23. Bozzette SA, Berry SH, Duan N, et al. The care of HIV-infected adults in the United States. HIV Cost and Services Utilization Study Consortium. *N Engl J Med.* Dec 24 1998;339(26):1897-1904.
24. Turner BJ, Cunningham WE, Duan N, et al. Delayed medical care after diagnosis in a US national probability sample of persons infected with human immunodeficiency virus. *Arch Intern Med.* Sep 25 2000;160(17):2614-2622.
25. Palacio H, Kahn JG, Richards TA, Morin SF. Effect of race and/or ethnicity in use of antiretrovirals and prophylaxis for opportunistic infection: a review of the literature. *Public Health Rep.* May-Jun 2002;117(3):233-251; discussion 231-232.
26. Shapiro MF, Morton SC, McCaffrey DF, et al. Variations in the care of HIV-infected adults in the United States: results from the HIV Cost and Services Utilization Study. *Jama.* Jun 23-30 1999;281(24):2305-2315.
27. Gebo KA, Fleishman JA, Conviser R, et al. Racial and gender disparities in receipt of highly active antiretroviral therapy persist in a multistate sample of HIV patients in 2001. *J Acquir Immune Defic Syndr.* Jan 1 2005;38(1):96-103.
28. Ghani AC, Donnelly CA, Anderson RM. Patterns of antiretroviral use in the United States of America: analysis of three observational databases. *HIV Med.* Jan 2003;4(1):24-32.
29. Ebrahim SH, Anderson JE, Weidle P, Purcell DW. Race/ethnic disparities in HIV testing and knowledge about treatment for HIV/AIDS: United States, 2001. *AIDS Patient Care STDS.* Jan 2004;18(1):27-33.
30. Wong MD, Cunningham WE, Shapiro MF, et al. Disparities in HIV treatment and physician attitudes about delaying protease inhibitors for nonadherent patients. *J Gen Intern Med.* Apr 2004;19(4):366-374.

31. Bangsberg DR, Hecht FM, Clague H, et al. Provider assessment of adherence to HIV antiretroviral therapy. *J Acquir Immune Defic Syndr*. Apr 15 2001;26(5):435-442.
32. Escaffre N, Morin M, Bouhnik AD, et al. Injecting drug users' adherence to HIV antiretroviral treatments: physicians' beliefs. *AIDS Care*. Dec 2000;12(6):723-730.
33. Miller LG, Liu H, Hays RD, et al. How well do clinicians estimate patients' adherence to combination antiretroviral therapy? *J Gen Intern Med*. Jan 2002;17(1):1-11.
34. Kleeberger CA, Buechner J, Palella F, et al. Changes in adherence to highly active antiretroviral therapy medications in the Multicenter AIDS Cohort Study. *Aids*. Mar 5 2004;18(4):683-688.
35. Heslin KC, Andersen RM, Ettner SL, Cunningham WE. Racial and Ethnic Disparities in Access to Physicians with HIV-related Expertise. Findings from a Nationally Representative Study. *Journal of General Internal Medicine*. 2005;20(3):283-289.
36. Stone VE, Mansourati FF, Poses RM, Mayer KH. Relation of physician specialty and HIV/AIDS experience to choice of guideline-recommended antiretroviral therapy. *J Gen Intern Med*. Jun 2001;16(6):360-368.
37. Sengupta S, Strauss RP, DeVellis R, Quinn SC, DeVellis B, Ware WB. Factors Affecting African-American Participation in AIDS Research. [Miscellaneous Article]. *JAIDS Journal of Acquired Immune Deficiency Syndromes* July. 2000;24(3):275-284.
38. Corbie-Smith G, St George DM, Moody-Ayers S, Ransohoff DF. Adequacy of reporting race/ethnicity in clinical trials in areas of health disparities. *J Clin Epidemiol*. May 2003;56(5):416-420.
39. Shavers-Hornaday VL, Lynch CF, Burmeister LF, Torner JC. Why are African Americans under-represented in medical research studies? Impediments to participation. *Ethn Health*. Mar-Jun 1997;2(1-2):31-45.
40. Corbie-Smith GM. The Continuing Legacy of the Tuskegee Syphilis Study: Considerations for Clinical Investigation. [Article]. *American Journal of the Medical Sciences* January. 1999;317(1):5-8.
41. Corbie-Smith G, Moody-Ayers S, Thrasher AD. Closing the circle between minority inclusion in research and health disparities. *Arch Intern Med*. Jul 12 2004;164(13):1362-1364.
42. Roberson NL. Clinical trial participation. Viewpoints from racial/ethnic groups. *Cancer*. Nov 1 1994;74(9 Suppl):2687-2691.
43. Corbie-Smith G, Miller WC, Ransohoff DF. Interpretations of 'appropriate' minority inclusion in clinical research. *Am J Med*. Feb 15 2004;116(4):249-252.
44. NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research. October 2001;  
[http://grants.nih.gov/grants/funding/women\\_min/guidelines\\_amended\\_10\\_2001.htm](http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm). Accessed June 2, 2006, 2006.



45. Ross S, Grant A, Counsell C, Gillespie W, Russell I, Prescott R. Barriers to participation in randomised controlled trials: a systematic review. *J Clin Epidemiol.* Dec 1999;52(12):1143-1156.
46. Freimuth VS, Quinn SC, Thomas SB, Cole G, Zook E, Duncan T. African Americans' views on research and the Tuskegee Syphilis Study. *Soc Sci Med.* Mar 2001;52(5):797-808.
47. Arcan PA, Perri MG, Nezu AM, Schein RL, Christopher F, Joseph TX. Comparative effectiveness of social problem-solving therapy and reminiscence therapy as treatments for depression in older adults. *J Consult Clin Psychol.* Dec 1993;61(6):1003-1010.
48. Corbie-Smith G, Thomas SB, Williams MV, Moody-Ayers S. Attitudes and beliefs of African Americans toward participation in medical research. *J Gen Intern Med.* Sep 1999;14(9):537-546.
49. Corbie-Smith G, Viscoli CM, Kernan WN, Brass LM, Sarrel P, Horwitz RI. Influence of race, clinical, and other socio-demographic features on trial participation. *J Clin Epidemiol.* Apr 2003;56(4):304-309.
50. Khaliq W, Gross M, Thyagarajan B, Jones-Webb R. What motivates minorities to participate in research? *Minn Med.* Oct 2003;86(10):39-42.
51. Shavers VL, Lynch CF, Burmeister LF. Racial differences in factors that influence the willingness to participate in medical research studies. *Ann Epidemiol.* May 2002;12(4):248-256.
52. Shavers VL, Lynch CF, Burmeister LF. Factors that influence African-Americans' willingness to participate in medical research studies. *Cancer.* Jan 1 2001;91(1 Suppl):233-236.
53. Corbie-Smith G, Thomas SB, St George DM. Distrust, race, and research. *Arch Intern Med.* Nov 25 2002;162(21):2458-2463.
54. Stone VE, Mauch MY, Steger K, Janas SF, Craven DE. Race, Gender, Drug Use, and Participation in AIDS Clinical Trials Lessons from a Municipal Hospital Cohort. *Journal of General Internal Medicine.* 1997;12(3):150-157.
55. Mills E, Wilson K, Rachlis B, et al. Barriers to participation in HIV drug trials: a systematic review. *Lancet Infect Dis.* Jan 2006;6(1):32-38.
56. Hall MA, Camacho F, Dugan E, Balkrishnan R. Trust in the medical profession: conceptual and measurement issues. *Health Serv Res.* Oct 2002;37(5):1419-1439.
57. Warner TD, Roberts LW, Nguyen K. Do psychiatrists understand research-related experiences, attitudes, and motivations of schizophrenia study participants? *Compr Psychiatry.* May-Jun 2003;44(3):227-233.
58. Daugherty C, Ratain MJ, Grochowski E, et al. Perceptions of cancer patients and their physicians involved in phase I trials. *J Clin Oncol.* May 1995;13(5):1062-1072.
59. Advani AS, Atkeson B, Brown CL, et al. Barriers to the participation of African-American patients with cancer in clinical trials: a pilot study. *Cancer.* Mar 15 2003;97(6):1499-1506.

60. Colfax G, Buchbinder S, Vamshidar G, et al. Motivations for participating in an HIV vaccine efficacy trial. *J Acquir Immune Defic Syndr*. Jul 1 2005;39(3):359-364.
61. Buchbinder SP, Metch B, Holte SE, Scheer S, Coletti A, Vittinghoff E. Determinants of enrollment in a preventive HIV vaccine trial: hypothetical versus actual willingness and barriers to participation. *J Acquir Immune Defic Syndr*. May 1 2004;36(1):604-612.
62. Tello J, Soong SJ, Hunter B, Meriwether R, Hook EW, 3rd, Mulligan MJ. HIV vaccine acceptance among heterosexual clients of a sexually transmitted diseases clinic. *Am J Med Sci*. Jan 1998;315(1):11-16.
63. Anjali S. Advani MD, Benjamin Atkeson MD, Carrie L. Brown BA, et al. Barriers to the Participation of African-American Patients with Cancer in Clinical Trials. *CANCER*. 2003;97(6):1499-1506.
64. Brown EJ. Recruitment Feasibility and HIV Prevention Intervention Acceptability Among Rural North Florida Blacks. *Journal of Community Health Nursing*. Fall 2002;19(3):147-160.

## List of Tables

Table 1. Evidence Table for Vu, Steketee, Valleroy, et al., 2002.

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Assessment & Weighting of Methodological Quality	Important Results	Conclusions
<p>Vu, M. Q., R. W. Steketee, Valleroy, et al., 2002.</p> <p>To summarize HIV incidence patterns and trends in the U.S.</p>	Systematic Review	<p>Minimal</p> <p>-Very systematic literature search with appropriate inclusion/exclusion criteria</p>	<p>Minimal</p> <p>-Different methods for incidence calculation used among included studies</p>	<p>Poor</p> <p>-No mention of assessing the quality of the studies included in their analysis, nor weighting them based on their overall quality</p> <p>-Scarcity of data available may make this less important</p>	<p><u>MSM</u></p> <p>-Early incidence very high from late 1970s to mid 1980s (as high as 20/100 p-y)</p> <p>-Downward trend begins ~mid 1980s (3-11/100 p-y)</p> <p>-Stabilized incidence in 1990s ~2-4/100 p-y</p> <p>-Consistently higher incidence than any other risk group across time</p> <p><u>IDU</u></p> <p>-Incidence patterns varied widely by region &amp; time</p> <p>-NY as high as 7/100 p-y in 1984 and has trended towards 1-2/100 p-y in 1990s</p> <p>-Philadelphia stable 3-4/100 p-y in late 80s to 1990s</p> <p>-Baltimore stable 4-5/100 p-y from late 80's to present</p> <p>-Chicago 8-9/100 p-y in late 80s to 1-3/100 p-y in 1990s</p> <p>-Western U.S. max of ~4/100 p-y in late 80s, trending downwards in 90s</p> <p><u>STD Clinics</u></p> <p>-Very few studies</p> <p>-2-3/100 p-y in early 1990s</p> <p>-&lt;1/100 p-y in late 1990s</p> <p><u>Commercial Sex Workers</u></p> <p>-Very few studies</p> <p>-12-19/100 p-y in Florida, late 1980s</p>	<p>Fair</p> <p><u>MSM</u></p> <p>-Decrease in mid 1980s may be from increased prevention efforts and/or those w/ most high-risk activity may have already been infected</p> <p><u>IDU</u></p> <p>-Peaked in mid 80s and decreased to &lt;2/100 p-y by late 1990s</p> <p>-Decreased incidence in N.E. cities during 1990s</p> <p>-Higher incidence in Eastern U.S. than Western U.S., as in MSM</p> <p>-Certain high risk populations have high incidences, but incidence among low risk groups such as military, blood donors, or general population remain low</p>

Table 2. Evidence Table for Harawa, Douglas, McFarland, et al., 2004

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Con-founding	Important Results	Conclusions
<p><b>Harawa, N.T., Douglas, J., 2004</b></p> <p>To study temporal changes in epidemiology of HIV in STD clinics in 4 western , urban U.S. counties from 1989 to 1999.</p>	Serial cross-sectional Design	<p><b>Minimal/Moderate</b></p> <ul style="list-style-type: none"> <li>-Seattle Clinic had sliding scale fees but others had none (less of a problem since they contribute the least patients)</li> <li>-Sampling times and durations varied by site</li> </ul>	<p><b>Moderate</b></p> <ul style="list-style-type: none"> <li>-Used two different tests over study period? (likely identical usage across study sites makes this less of a problem)</li> <li>-30-40% of those eligible lacked a blood sample, compared to &lt;10% in other 3 counties (Seattle also had the least # of patients, making this less of a problem)</li> <li>-L.A. did not include all public STD clinics in study</li> </ul>	<p><b>Moderate</b></p> <ul style="list-style-type: none"> <li>-Large demographic differences in Table 1, likely reflect regional differences and not selection bias</li> <li>-MSM data adjusted for age, race, IDU status</li> <li>-Clinic population shifts</li> <li>-Difference in clinic presentation (care seeking) by race</li> <li>-Varying enrollment times and durations within and between sites could influence # of cases detected</li> </ul>	<p><b>1989-1990</b></p> <ul style="list-style-type: none"> <li>-Cum Prev ~2% in all counties but S.F. (9.3%)</li> <li>-Cum Prev highest in those &gt;30 years of age</li> <li>-Cum Prev highest for black MSW</li> <li>-MSW and Women who IDU were 2-10X more likely to have HIV</li> </ul> <p><b>Temporal Trends</b></p> <p>MSW</p> <ul style="list-style-type: none"> <li>-Prev declined at least 50% across all counties</li> <li>-Prev declined for all races (except whites in Seattle) and IDU across all sites</li> </ul> <p>Women</p> <ul style="list-style-type: none"> <li>-Prev declined at least 30% across 3 of 4 counties</li> <li>-Downward trend inconsistent across racial groups</li> <li>-Prev unchanged or increased in women &gt;40 y.o. in L.A. and S.F.</li> </ul> <p>MSM</p> <ul style="list-style-type: none"> <li>-Prev declined across all counties</li> <li>-Prev decline not as large or significant for Blacks</li> </ul>	<p><b>Overall Quality: Fair</b></p> <ul style="list-style-type: none"> <li>-MSMs comprise a higher proportion of HIV burden in western states</li> <li>-Recent MSM prev is comparable w/ prev in other U.S. regions</li> <li>-Reduction in Western MSM prev has been less among Blacks than among Whites</li> <li>-Less generalizable for other U.S. regions, general clinic patients, and STD clinic patients not having new STD complaint or routine STD evaluation</li> </ul>

Table 3. Evidence Table for Calonge, Petersen, Miller, Marshall, 2003.

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p><b>Calonge, Petersen, Miller, Marshall, 2003.</b></p> <p>To estimate the seroprevalence of HIV-1 infection in persons seeking care from primary health care providers from June 1, 1989 to December 31, 1990.</p>	Cross-sectional	<p><b>Minimal</b></p> <ul style="list-style-type: none"> <li>-Patients from ASPN database don't differ substantially from U.S. gen. population in age or gender</li> <li>-Variable enrollment schedules by practice (controlled for in analysis)</li> <li>-93% of original sample included in final analysis</li> <li>-Are only patients who had blood drawn</li> <li>-87% of patients White American (but likely characterizes clinic population)</li> </ul>	<p><b>Moderate</b></p> <ul style="list-style-type: none"> <li>-Dependent on assay—not adequately discussed</li> </ul>	<p><b>Minimal</b></p> <ul style="list-style-type: none"> <li>-Fewer men &lt;30y.o. than for gen. population</li> <li>-More women &gt;20y.o. than for gen. U.S. population</li> <li>-For men &lt;40 y.o., are fewer in sample than in NAMCS population for general practitioners</li> <li>-For women &gt; 20 y.o., are more in sample than in NAMCS population</li> </ul>	<ul style="list-style-type: none"> <li>-Overall Seroprevalence 2.3/1000 (95%CI 1.3-3.3)</li> <li>-Previously Unrecognized Seroprev. 1.0/1000 (95%CI 0.3-1.7).</li> <li>-57% of men were previously unrecognized, compared to 33% of women</li> <li>-Men had 4X higher seroprevalence than women (4.6 vs. 1.2 per 1000 p-y)</li> <li>-4.5 vs. 1.3/1000 p-y prevalence for non-rural vs. rural practices</li> </ul>	<p><b>Overall Quality: Good</b></p> <ul style="list-style-type: none"> <li>-Fits in with existing literature of that time cited as ranging from 0.42-3.6/1000 in HIV prevalence among various different risk groups</li> <li>-Men's seroprevalence may be under-estimated and women's seroprevalence may be over-estimated given sex demographics in comparison to NAMCS data.</li> <li>May not be generalizable to broad clinic populations—only populations whom have blood drawn</li> <li>Not generalizable to general population b/c not all seek care</li> <li>Not generalizable to those outside of age range 15-49.</li> <li>87% White study population—may not generalize in other races</li> </ul>

Table 4. Evidence Table for Pincus, Crosby, Losina, et al., 2003.

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p><b>Pincus, Crosby, Losina, et al., 2003</b></p> <p><b>To determine prevalence of acute HIV infection among patients with symptoms of a viral illness who presented to an urgent care center at an urban teaching hospital from March 30, 2000 to March 30, 2001.</b></p>	Cross-sectional	<p><b>Minimal</b></p> <p>-36.5% enrollment rate (of all screened at triage)</p> <p>-93.3% of those deemed eligible were enrolled</p>	<p><b>Minimal</b></p> <p>-Measurement of cases dependent on test characteristics</p> <p>-Used most sensitive assay for HIV detection w/ no false positives</p>	<p><b>Minimal b/c</b> although some unequal demographics, may reflect characteristics of target population</p> <p>-Unequal sex (more men), race (more African Americans), and sexual practices (80% had any sex)</p>	<p>-Total HIV prevalence 2.2% (95%CI 0.9-3.5)</p> <p>-Acute HIV prevalence 1.0% (95%CI 0.1-1.9)</p> <p>-Chronic HIV prevalence 1.2% (95%CI 0.2-2.2)</p> <p>-Lowest possible acute HIV prevalence is 0.6%</p>	<p><b>Overall Quality: Good</b></p> <p>-Demographics of study site similar to 72 other hospitals in the U.S.</p> <p>-Prevalence of acute and chronic HIV obtained for this study similar to results from previous studies</p> <p>-Not generalizable to those with no signs/symptoms of viral illness, to those w/o risk factors, to general populations, to those w/ chronic HIV infection</p>

Table 5. Evidence Table for Coco and Kleinhans, 2005.

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p><b>Coco and Kleinhans, 2005.</b></p> <p>To calculate a national estimate of the prevalence of primary HIV infection for patients visiting physicians' offices, emergency departments, and hospital outpatient clinics with symptoms consistent with primary HIV infection regardless of risk factors for the year 2000.</p>	Cross-sectional	<p><b>Minimal</b></p> <p>-Denominator includes patients with up to 3 symptoms consistent w/ acute HIV and excludes those w/ symptoms less likely to be HIV (ex. all 3 symptoms had to be consistent w/ HIV)</p> <p>-Numerator accounted for % of all HIV accounted for in denominator, % of cases w/ symptoms, % of cases who seek care</p>	<p><b>Minimal</b></p> <p>-Measurement of HIV and of symptoms (denominator) subject to quality of data collection for the NAMCS and NHAMCS databases</p> <p>-Assumptions for numerator are reproducible and logical, but dependent upon quality of data supporting them</p> <p>-Great uncertainty in estimation of percentage seeking care, but sensitivity analysis done</p>	<b>Minimal</b>	<p><b><u>Prevalence Estimates</u></b></p> <p>Fever 0.66% (95%CI 0.53-0.92)</p> <p>Rash 0.56% (95%CI 0.35-0.94)</p> <p>Pharyngitis  0.13% (95%CI 0.10-0.19)</p>	<p><b>Overall quality: Good</b></p> <p>Not generalizable to those &gt;54 y.o., federal, veteran, and military outpatient facilities, and those w/ undiagnosed chronic HIV infection</p>

Table 6. Evidence Table for Smith, Gwinn, Selik, et al., 2000.

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Assessment & Weighting of Methodological Quality	Important Results	Conclusions
<p>Smith, D.K., Gwinn, M., Selik, R.M., et al., 2000.</p> <p>To review the most current data on the extent of HIV infection and associated risk behaviors, the occurrence of AIDS, and HIV-related mortality in African Americans and suggest additional information, services, and intervention strategies to reduce HIV infection in this population.</p>	Systematic Review	<p><b>Moderate</b></p> <ul style="list-style-type: none"> <li>-Used computerized search and reviewed references lists of papers</li> <li>-Description of search methods vague and incomplete</li> <li>-Did not ask experts for additional papers</li> <li>-Did not explain methods for acquiring unpublished data, but several such sources used.</li> </ul>	<p><b>Minimal</b></p> <ul style="list-style-type: none"> <li>-Many different epidemiologic measures reported, but are important, meaningful, and consistent with objectives.</li> </ul>	<p><b>Very little</b></p> <ul style="list-style-type: none"> <li>-Appears data from papers only included if externally valid to U.S. Black HIV/AIDS population</li> </ul>	<p><b>HIV Incidence</b> 1985-1991: Estimated Seroincidence of 51.1 vs. 3.7 per 100,000 p-y for Black and White Americans, respectively. 1998: 6346 and 5015 new HIV cases for Black &amp; White Men, respectively. 4230 and 1268 new HIV cases for Black &amp; White Women, respectively.</p> <p><b>HIV Prevalence</b> 1988-1994: Seroprevalence of 1.10% and 0.20% for Black and White Americans 18-59 y.o., respectively. 1996: Seroprevalence for Black and White men age 16-21 are 0.22% and 0.04%, respectively. Seroprevalence for Black and White women age 16-21 are 0.35% and 0.07%, respectively.</p> <p><b>AIDS Incidence</b> 1998: Black and White Americans were 45.1% and 33.4% of all incident cases, respectively.</p> <p><b>HIV/AIDS Mortality</b> 1998: Estimated mortality rate of 58.2 and 9.8 per 100,000 for Black &amp; White men aged 25-44, respectively. Estimated mortality rate of 25.6 and 1.9 per 100,000 for Black &amp; White women aged 25-44, respectively.</p> <p><b>Census</b> 1998: African American – 12% White American – 72%</p>	<p><b>Overall Quality: Fair</b></p> <p>African Americans have the highest HIV and AIDS incidence, HIV prevalence, HIV mortality, and greatest number of years of potential life lost.</p> <p>Socioeconomic status does not entirely account for disparity in HIV/AIDS.</p> <p>Sexual networks may play a role in the disparate HIV transmission. More research is needed.</p> <p>More epidemiological studies are needed with generalizable samples and sample sizes sufficient for subanalyses.</p>



Table 7. Evidence Table for Rosenberg and Biggar, 1998.

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Con-founding	Important Results	Conclusions
<p><b>Rosenberg, P.S. and Biggar, R.J., 1998.</b></p> <p>To estimate trends in HIV incidence and prevalence in teenagers and young adults in 1988 and 1993.</p>	<p>Back Calculation to estimate the incidence of infection by working backward from AIDS surveillance data on the basis of the natural history.</p>	<p><b>Minimal</b></p> <p>-Only cases reported to CDC are used—corrected for this</p>	<p><b>Moderate</b></p> <p>-Possible misclassification bias for mode of transmission -CDC data for 1987-defined AIDS opportunistic illnesses are estimates and may be imprecise -Natural history could vary across risk groups—faster progression than estimated could result in HIV incidence being too high</p>	<p><b>Minimal</b></p> <p>-Patient or physician inappropriately suspecting homosexual activity when reporting (esp. during early epidemic)</p>	<p>1995: Black men and women had highest incidence of AIDS (124 per 100,000 and 60 per 100,000 respectively). White men and women had AIDS incidence rates of 23 and 5 per 100,000, respectively.</p> <p>Incidence of HIV was higher for young minority men than in young white men for all modes of transmission.</p> <p>Incidence of HIV was higher in young minority women than white women for injection drug use and heterosexual contact.</p> <p>The overall number of HIV cases decreased by 45% in white men, increased slightly in black men, and decreased slightly in Hispanic men from 1988-1993 among those age 23-27.</p>	<p><b>Overall Quality: Fair</b></p> <p>-Notable success in HIV prevention for white men (50% reduction in prevalence) -Prevalence in young black &amp; Hispanic men stable b/c increased incidence in teenagers and heterosexuals offset reductions in homosexual men and injection drug users in their 20's -Increasing HIV prevalence among women aged 20-25 from increased heterosexual transmission -From 1983 to 1993, blacks comprised an increasingly significant proportion of all estimated HIV cases (my own conclusion)</p>

Table 8. Evidence Table for Dean, Steele, Satcher, & Nakashima, 2005

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Con-founding	Important Results	Conclusions
<p>Dean, H.D., Steele, C.B., Satcher, A.J., and Nakashima, A.K., 2005.</p> <p>To examine the HIV epidemic among minority races and ethnicities in the US</p>	<p>Analysis of National Survei-llance Data</p>	<p><b>Moderate</b></p> <p>-HIV Data: Only from 32 states using name-based reporting of HIV infection since at least 1999</p> <p>-32 states account for 57% of US population and 44% of all AIDS diagnoses in the US</p> <p>-Omits NY, IL, &amp; Ca</p> <p>-Cases must be reported to be measured (many not tested or tested anonymously—which aren't reported)</p>	<p><b>Minimal</b></p> <p>-Recent diagnoses aren't necessarily new cases</p>	<p><b>Moderate</b></p> <p>-Those of lower SES may be screened or tested at higher or lower rates than those of higher SES</p> <p>-Those of lower SES may be more likely to be reported</p>	<p>-From 2000-2003 in the 32 states, 45% of male HIV/AIDS cases &amp; 69% of female cases were black</p> <p>-HIV/AIDS diagnosis rate was 74/100,000 for blacks and 9/100,000 for whites</p> <p>-AIDS diagnoses rates in 2003 were approximately 8 and 13 times higher for black males and females than white males and females, respectively.</p> <p>-Blacks accounted for 53% of estimated deaths among those with AIDS</p>	<p><b>Overall Quality: Fair</b></p> <p>-Minority races are disproportionately affected by HIV</p> <p>-Race &amp; ethnicity are not risk factors for HIV, but markers for socioeconomic factors</p> <p>-Given the high HIV prevalence in the black community, even "low-risk behavior" can pose a higher threat of HIV than in communities with a lower prevalence</p> <p>-This analysis may be used to direct prevention activities, such as the Minority HIV/AIDS Research Initiative (MARI), Sisters Informing Sisters about Topics on AIDS (SISTA), and Advancing HIV Prevention (AHP) initiative</p>

Table 9. Evidence Table for:

CDC. Trends in HIV/AIDS Diagnoses -- 33 States, 2001-2004. 2005.

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Con-founding	Important Results	Conclusions
<p>Center for Disease Control &amp; Prevention, 2005.</p> <p><u>Trends in HIV/AIDS Diagnoses – 33 States, 2001-2004.</u></p> <p>To measure trends in HIV/AIDS Diagnoses from 2001-2004.</p>	<p>Analysis of National Surveillance Data</p>	<p><b>Moderate</b></p> <p>Only used data from 33 states using name-based reporting (estimated to represent only 63% of all AIDS cases in US during 2001-2004)</p> <p>California is not included</p>	<p><b>Minimal</b></p> <p>-Recent diagnoses aren't necessarily new cases</p>	<p><b>Moderate</b></p> <p>-New addition of NY data is large enough to change estimates of incidence/prevalence when compared to previous reports from CDC</p> <p>-Recent changes in reporting requirements</p>	<p>Blacks accounted for 51% of persons with HIV/AIDS diagnosed (68% among females and 44% among males)</p> <p>-29% were white, 18% were Hispanic</p> <p>-Non-statistically significant decrease in HIV/AIDS diagnoses from 2001 to 2004.</p> <p>-5.0% average annual decrease in rates among blacks</p>	<p><b>Overall Quality: Fair</b></p> <p>Decreased rates among black could be from differential change in testing patterns among various populations, decreased incidence of HIV infections, or the effect of additional data added to the national surveillance system</p>

Table 10. Evidence Table for: Ross, Grant, Counsell, et al., 1999

Author, Year, Study Question	Study Design	Potential for Selection or Publication Bias	Potential for Measurement Bias	Assessment & Weighting of Methodological Quality	Important Results	Conclusions
<p>Ross, S., Grant, A., Counsell, C., et al., 1999.</p> <p>To systematically review barriers to clinician and patient participation in randomized trials.</p> <p>To make recommendations for improving the conduct of trials based on the findings.</p>	<p>-Systematic Review of studies from 1986 to 1996.</p> <p>-Identified 9732 references</p> <p>-265 of these identified clinician or patient participation as an important issue</p> <p>-78 of these reported original empirical evidence</p>	<p><b>Moderate</b></p> <p>-Searched Medline, Embase, and CINAHL</p> <p>-Do not discuss search strategy</p> <p>-Do not discuss any attempts to acquire unpublished data</p> <p>-Majority of papers are from Cancer research, the U.S., and are hospital based</p>	<p><b>Significant potential for bias</b></p> <p>-No discussion of inter-rater agreement</p>	<p><b>Poor</b></p> <p>-Reported inclusion/exclusion criteria for abstracts</p> <p>-Two reviewers extracted data from articles independently.</p> <p>-No discussion of assessing internal validity</p> <p>-Methods for systematically reviewing qualitative studies are still in development</p>	<p>-Potential barriers to patients were patient concerns such as additional demands on patient, patient preferences for a particular treatment, worry about uncertainty of treatment or trials, and patient concerns about information and consent.</p> <p>-Physician concerns hindering patient participation were protocol causing problems with recruitment, clinician concerns about information provision to patients, and clinician influencing patient decision not to join.</p>	<p><b>Internal Validity: Poor</b></p> <p><b>External Validity: Poor</b></p> <p>-To overcome barriers with clinician recruitment, RCTs should address an important question, have a clear and simple protocol, require as little as possible from the clinicians, and have straight-forward data collection. They should also include dedicated research staff to support clinical staff and favor pragmatic trial designs.</p> <p>-To overcome barriers with patient participation, demands of the study should be as minimal as possible, clear explanation of the extent and purpose of the study should be provided, and support for the decision to participate should be provided. Dedicated research staff should be used for providing information, obtaining patient consent, and monitoring the recruitment process.</p>

Table 11. Evidence Table for: Freimuth, Quinn, Thomas, et al., 2001

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p>Freimuth, V.S., Quinn, S.C., Thomas, S.B., et al., 2001.</p> <p>To examine knowledge of and attitudes toward medical research, knowledge of the Tuskegee Syphilis Study, and reactions to the HOME Box Office production, Miss Evers' Boys, a fictionalized version of the Tuskegee Study.</p>	<p>Qualitative Methods using seven focus groups of African Americans in four regions of the U.S.</p>	<p><b>Minimal</b></p> <ul style="list-style-type: none"> <li>-Targeted diverse populations for recruitment.</li> <li>-One moderate-income focus group in Chicago did not occur—may weaken external validity</li> </ul>	<p><b>Moderate</b></p> <ul style="list-style-type: none"> <li>-Don't discuss whether saturation was reached—may have missed important themes</li> </ul>	<p><b>Moderate</b></p> <ul style="list-style-type: none"> <li>-Previous knowledge of the Tuskegee study</li> <li>-Past participation in research</li> <li>-Limited demographic data for 8 of the 60 participants</li> </ul>	<ul style="list-style-type: none"> <li>-Accurate knowledge about research was limited</li> <li>-Lack of understanding and trust of informed consent procedures was problematic</li> <li>-Distrust of researchers posed a substantial barrier to recruitment</li> <li>-Participants felt research was important, but clearly distinguished between the types of research they would be willing to participate in and their motivations for doing so.</li> <li>-Many did not distinguish well between treatment, prevention, and research.</li> <li>-Privacy, Masking, and trust were important in affecting willingness to participate</li> </ul>	<p><b>Internal Validity: Fair</b>  <b>External Validity: Limited due to small sample size and unconfirmed saturation. Geographic diversity is a strength, however.</b></p> <ul style="list-style-type: none"> <li>-Measures to increase participants' understanding of informed consent and research procedures are necessary. This should involve methods to improve individual studies' communication to participants as well as a mass communication campaign about research.</li> <li>-Increasing trust between African Americans and researchers is also paramount. Researchers should address concerns about scientific misconduct proactively, factually, and clearly.</li> <li>-Merely including minority researchers and staff is not sufficient to increase minority recruitment. Professional programs in the Schools of medicine and public health should include preparation about culture, race and class, and working with diverse populations.</li> </ul>

Table 12. Evidence Table for Shavers, Lynch, & Burmeister, 2002

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p>Shavers, V.L., Lynch, C.F., Burmeister, S.F., 2002.</p> <p>-Also see their 2001 publication.</p> <p>To examine racial difference in the prevalence of sociocultural barriers as a possible explanation for the underrepresentation of African Americans in medical research studies</p>	<p>Cross-sectional survey of the Detroit Primary Metropolitan Statistical Area during 1998-1999.</p>	<p><b>Moderate</b></p> <p>-Differential non-coverage bias from old census (greater in suburbs than city)</p> <p>-36% Response rate</p>	<p><b>Minimal</b></p> <p>-Two different survey techniques-- Mail vs. telephone (differential bias)</p> <p>-Is survey validated or pilot tested?</p>	<p><b>Moderate</b></p> <p>-Survey technique used per participant</p> <p>-Sex, education, income, age</p>	<p>-Education associated with willingness to participate in a medical research study (<math>p=0.05</math>).</p> <p>-Among respondents who believed that minorities bore the greatest burden of medical research risks, 55% of blacks compared to 88% of whites indicated that they'd be willing to participate in medical research (<math>p=0.05</math>).</p> <p>-66% of blacks vs. 42% of whites reported that the poor bear most of the risks of medical research (<math>p=0.04</math>)</p> <p>-81% and 28% of blacks and whites, respectively, were aware of the Tuskegee study (<math>p=0.01</math>).</p> <p>-49% of blacks vs. 17% of whites that reported that their knowledge of Tuskegee would affect their future participation indicated an unwillingness to participate (<math>p=0.05</math>).</p> <p>-In multivariate analysis of blacks, only knowledge of Tuskegee Study and changes in trust of medical researchers due to this knowledge were significantly associated with future willingness to participate in medical research. After adjusting for changes in trust, blacks who knew about the Tuskegee Study were more likely than those who didn't to be willing to participate in a medical research study in the future (OR = 464.4, 95% CI 44.4-486.4). Willingness was lower if effect of knowledge was a reduction in the level of trust of medical researchers (OR=0.21, 95% CI 0.07-0.98) when compared to no change in trust and increased level of trust.</p> <p>-Multivariate analysis for whites showed educational level and beliefs about racial sharing of medical research risks predicted their willingness to participate in medical research studies.</p>	<p><b>Internal Validity: Fair</b></p> <p><b>External Validity: Inner city &amp; suburban communities in Detroit—may not generalize to other geographic regions</b></p> <p>Different responses between races about medical research risk sharing suggest a failure to reconcile the belief that the poor bear a disproportionate burden of risks with the fact that racial minorities are disproportionately represented among the poor.</p> <p>-Having knowledge alone of the Tuskegee study does not seem to influence willingness to participate in research. Tuskegee's role appears to be its contribution to overall distrust of medical researchers among African Americans.</p>

Table 13. Evidence Table for: Corbie-Smith, Thomas, St. George, 2002

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p>Corbie-Smith, G., Thomas, S.B., St. George, D.M.M., 2002.</p> <p>To examine possible differences in distrust by race and to determine to what extent other sociodemographic factors explain any racial differences in distrust.</p>	<p>Cross-sectional survey of 909 individuals of black and white race in the U.S.</p> <p>Sampling design appears to be case-control, but analyses were done according to race—ignoring the original sampling design.</p> <p>Sample weighted to be nationally representative.</p>	<p><b>Moderate</b></p> <p>-Had to have phone -Refusal rate similar for two sample groups (49.6%)</p>	<p><b>Minimal</b></p> <p>-Constructed a validated scale for distrust outcome measure. -Sensitivity analyses done w/ different categorical cutoffs of outcome variable and w/ outcome as a continuous variable.</p>	<p><b>Minimal</b></p> <p>-Assessed for effect modification -Controlled for possible confounders: education, employment, and region</p>	<p>-Age, Education, Employment, Income and Region were significantly associated with race. -Race, sex, education, employment, and region were significantly associated with distrust. -Education, Employment, and Region considered confounders in multivariate analysis -African Americans have a higher prevalence of distrust than Whites (<math>p &lt; 0.01</math>). -When adjusted for covariates, African Americans have more odds of having distrust than Whites (OR=4.7, 95% CI 2.9-7.7).</p>	<p><b>Internal Validity: Good</b> <b>External Validity: Generalizes well to general U.S. population, but sampling techniques may have excluded the very poor or the very busy.</b></p> <p>After adjusting for markers of social class, African Americans are still less trusting of medical researchers than Whites. SES only had a small effect on distrust (6%). -Recruitment in African American community should be thought of as a process of ongoing engagement, dialogue, and feedback.</p>

Table 14. Evidence Table for: Stone, Mauch, Steger, 1997

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p>Stone, V.E., Mauch, M.Y., Steger, K., et al., 1997.</p> <p>To determine whether participation rates of women, persons of color, and injection drug users in AIDS clinical trials are similar to those of other HIV/AIDS patients.</p> <p>To examine whether differences in patients' knowledge of clinical trials or reasons for not participating explain differences in participation rates by gender, race, or drug use.</p>	<p>Cross-Sectional survey of symptomatic HIV patients receiving ongoing ambulatory care at a municipal teaching hospital.</p>	<p><b>Minimal</b></p> <p>-Don't tell how acquired convenience sample.</p>	<p><b>Moderate</b></p> <p>-Didn't test for interaction for one variable</p> <p>-Possible race concordance with interviewer</p>	<p><b>Moderate</b></p> <p>-Race concordance of interviewer</p> <p>-Learning of trials elsewhere</p> <p>-Knowledge Outcome: could be confounded by race concordance of clinic staff, education, dementia, or disease severity</p>	<p>-Sex, Race, Injection drug use, and disease severity stat. significantly associated with clinical trial participation.</p> <p>-Race and injection drug use remain significant after adjustment for disease severity, age, education, and clinic type.</p> <p>-Sex and race stat. associated with being kept informed of new HIV treatments and experimental drugs and being told of clinical trials for which they are eligible.</p> <p>-For most commonly cited reasons of nonparticipation, race was stat. significantly associated with disinterest or not wanting to participate and non-eligibility.</p>	<p><b>Internal Validity: Fair</b></p> <p><b>External Validity: Generalizable to urban minority patients who are poor, in care, and symptomatic.</b></p> <p>-Persons of color and injection drug users were significantly less likely to participate in clinical trials than others with HIV despite the presence of on-site clinical trials.</p> <p>-Persons of color were less than half as likely to cite ineligibility as their reason for not participating, twice as likely to report lack of interest as their reason for not participating, and less likely to report being informed of clinical trials. Thus, non-whites do not perceive their lack information as an important determinant in their decision to participate.</p> <p>-Efforts that go beyond placement of AIDS clinical trials units in underserved areas are necessary.</p> <p>-There is a great need to educate all HIV/AIDS patients and their physicians about clinical trials and their participation.</p>



Table 15. Evidence Table for: Mills, Wilson, Rachlis, et al., 2006

Author, Year, Study Question	Study Design	Potential for Selection or Publication Bias	Potential for Measurement Bias	Assessment & Weighting of Methodological Quality	Important Results	Conclusions
<p>Mills, E., Wilson, K., Rachlis, B., et al., 2006</p> <p>To systematically review the literature on barriers and concerns among HIV patients to participation in HIV clinical drug trials.</p>	<p>-Systematic Review of qualitative and quantitative studies.</p> <p>Searched AMED, Campbell, CINAHL, Cochrane Library, Embase, ERIC, Medline, and UK National Health Service Economic Evaluation Database.</p>	<p><b>Minimal</b></p> <p>-Sought unpublished studies from ClinicalTrials.gov and UK National Research Register</p> <p>-Report inter-rater agreement for selection of papers</p>	<p><b>Moderate</b></p> <p>-No discussion of inter-rater agreement for appraisal of internal validity</p>	<p><b>Good</b></p> <p>-2 reviewers independently reviewed abstracts &amp; papers for eligibility, data extraction, and appraisal of validity</p> <p>-Used checklist to assess internal validity</p> <p>-Report inclusion/exclusion criteria</p>	<p>-Major barriers to participation included fear of side-effects, distrust of researchers, general concerns about research design, interference in everyday life or changes in routine, and social discrimination.</p> <p>-Quantitative studies indicated that the most prevalent barriers were: suspicions about the drug itself (53%, 95% CI 27-83%), patients were not informed or believed they were not eligible (38%, 25-50%), and travel or transport obstacles (39%, 21-57%).</p>	<p><b>Internal Validity: Good</b></p> <p><b>External Validity: Medium to high income nations</b></p> <p>-The informed consent process should be used to address the important issues raised in this review</p> <p>-Researchers should clearly communicate intentions and involve local investigators and the HIV community in the research process</p> <p>-Investigators should clearly articulate means by which confidentiality is protected and adopt culturally sensitive and non-traditional changes to facilitate participation by those typically under-represented.</p>

Table 16. Evidence Table for: Tello, Soong, Hunter, et al., 1998

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p>Tello, J., Soong, S., Hunter, B., et al., 1998.</p> <p>To evaluate the willingness of heterosexual STD clinic clients to participate in clinical trials of vaccines to prevent HIV-1 infection.</p>	<p><b>Cross-sectional</b></p> <p>Convenience Sample from an STD Clinic in Birmingham, AL</p>	<p><b>Moderate</b></p> <p>-Sampling method may be systematic/non-random</p> <p>-Only 4 refused to participate</p> <p>-&gt;50% had current STD symptoms</p>	<p><b>Minimal</b></p> <p>-No mention of pilot-testing survey</p> <p>-Recall bias</p>	<p><b>Moderate</b></p> <p>-Reason for visit is a potential confounder</p> <p>-Adjusted for age, gender, race, previous STD treatment, previous gonorrhea history, previous genital herpes history, knowledge of friends or relatives with HIV-1 infection, previous HIV-1 testing, number of sex partners in lifetime, use of crack cocaine, and use of intravenous drugs</p>	<p>-67% of sample willing to participate.</p> <p>-Those previously tested for HIV-1 were more willing to participate in an HIV vaccine trial than those never tested (<math>p=0.04</math>).</p> <p>-More females were willing to participate than males (<math>p=0.08</math>).</p> <p>-Sex and previous testing for HIV-1 best predicted willingness to participate, <math>p=0.03</math> &amp; <math>p=0.05</math> respectively.</p>	<p><b>Internal Validity:</b> <b>Fair</b></p> <p><b>External Validity:</b> <b>Generalizable to large, urban STD clinics serving predominantly heterosexual, black populations</b></p> <p>-This sample is representative of the overall STD clinic.</p> <p>-Results are similar to or greater than many previously published willingness estimates</p> <p>-In this sample, those at highest risk of HIV-1 acquisition (men &amp; those never tested) were less willing to participate than those with less risk (women and those previously tested).</p>

Table 17. Evidence Table for: Corbie-Smith, Viscoli, Kernan, et al., 2003

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p>Corbie-Smith, G., Viscoli, C.M., Kernan, W.N., et al., 2003.</p> <p>-To examine the influence of race, other socio-demographic features, and clinical characteristics on the willingness of subjects to participate in a clinical trial.</p>	<p>Cross-Sectional analysis of those screened for participation in the Women's Estrogen for Stroke Trial (WEST) after June 1996.</p>	<p><b>Moderate</b></p> <p>-Did not measure those from 1993-May 1996.</p> <p>-988 potential subjects not screened b/c of physician refusal</p>	<p><b>Minimal</b></p> <p>-history of volunteerism has possible recall bias</p>	<p><b>Minimal</b></p> <p>-only controlled for education regarding SES— income not measured</p>	<p>- Age, history of volunteerism, nursing home residence, and referral from a physician were the socio-demographic features significantly associated with giving consent to participate</p> <p>-When stratified by race, employment was significant for black women and age, volunteerism, nursing home residence and referral were significant for white women as associated with consent to participate.</p> <p>-Hysterectomy, prior estrogen replacement therapy, MMSE score, and Diabetes were the clinical features significantly associated with giving consent.</p> <p>-When stratified by race, there were no significant associations for blacks, while hysterectomy, estrogen therapy, MMSE score, and diabetes were associated with consent to participate.</p> <p>-In the total cohort, age, hysterectomy, MMSE &gt; 24, volunteerism, and prior estrogen therapy were independently associated with consent to participate.</p> <p>-There were no significant associations for black women</p> <p>-Age, hysterectomy, MMSE &gt; 24, and volunteerism were independently associated with consent for white women.</p>	<p><b>Internal Validity: Fair</b></p> <p><b>External Validity: Post menopausal women w/ history of TIA or stroke in Connecticut</b></p> <p>-There was no difference in consent rates by race for the WEST cohort.</p> <p>-Younger age, h/o hysterectomy, prior estrogen therapy, volunteerism, and no cognitive impairment were predictors of consent.</p> <p>-Including sufficient minorities to represent their burden of disease may not yield participation rates high enough to definitively test differences by race. Such exploratory analyses are still valuable, however, for hypothesis generating and planning possible future studies in minority groups.</p>

Table 18. Evidence Table for: Buchbinder, Metch, Holte, et al., 2004

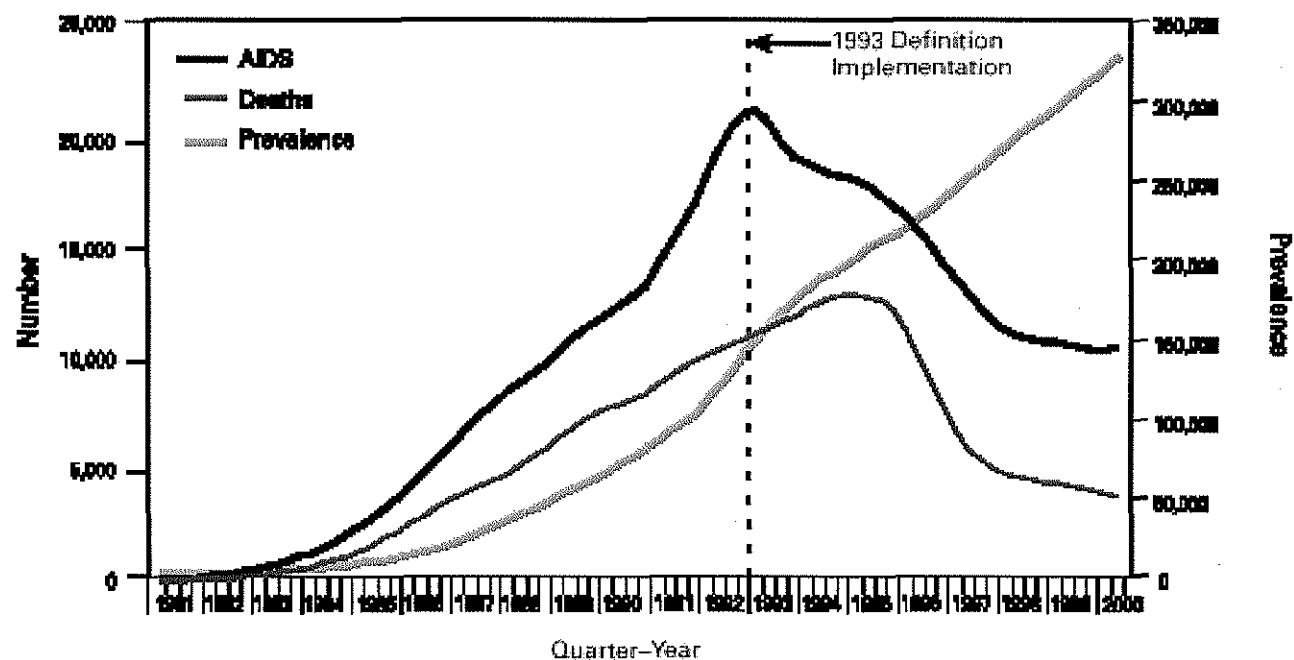
Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p><b>Buchbinder, S.P., Metch, B., Holte, S.E., et al., 2004</b></p> <p>To examine the relationship between hypothetical and actual willingness to enroll in an HIV vaccine trial.</p>	<p><b>Prospective Cohort</b></p> <p>Invited those previously enrolled in an HIV vaccine preparedness study (VPS) to be screened for eligibility for a phase 2 HIV vaccine trial.</p>	<p><b>Moderate</b></p> <ul style="list-style-type: none"> <li>-Excluded data from one site</li> <li>-Of the 2531 (attempted contact), 30% were unable to contact, did not finish the screening in time to consider enrollment, or had incomplete screening data.</li> <li>-Those unable to contact were stat. significantly different from those contacted for race, age, and injection drug use, HIV exposure, and # of sex partners at end of VPS</li> </ul>	<p><b>Minimal</b></p> <ul style="list-style-type: none"> <li>-Were those unable to contact actually "passive refusers?"</li> <li>-Risk behaviors and hypothetical willingness to participate were taken from past responses (non-differential)</li> </ul>	<p><b>Minimal</b></p> <ul style="list-style-type: none"> <li>-Adjusted Odds Ratios for site, demographic variables, risk group, and behavioral variables</li> </ul>	<ul style="list-style-type: none"> <li>-Stat. Significant association between hypothetical willingness and actual willingness (<math>p &lt; 0.001</math>).</li> <li>-Blacks more likely to refuse than Whites (adj OR=2.22, 95% CI 1.43-3.45)</li> <li>-Those with some college education are less likely to refuse participation than those with less than h.s. education (adj OR=0.44, 95% CI 0.23-0.85)</li> <li>-Age and No. of sex partners associated w/ actual willingness (unadj <math>p &lt; 0.001</math>)</li> <li>-Blacks cited concerns about trust, safety, trial logistics, and discomfort w/ study staff more than Whites.</li> <li>-Blacks cited concerns about having a positive antibody test often, but similar to other Whites.</li> <li>-Blacks cited concerns about reactions of others less than others.</li> <li>-94% cited altruistic reasons as primary motivator for trial participation.</li> </ul>	<p><b>Internal Validity: Good</b></p> <p><b>External Validity: Generalizable to diverse racial and risk groups with past participation in an HIV-related study</b></p> <ul style="list-style-type: none"> <li>- ~30% and ~50% of those who were definitely and probably willing to participate still refused to enroll. Past willingness was also significantly associated with ineligibility for the vaccine trial. Thus, past willingness not a perfect tool for predicting future enrollment.</li> </ul>

Table 19. Evidence Table for: Colfax, Buchbinder, Vamshidar, et al., 2005.

Author, Year, Study Question	Study Design	Potential for Selection Bias	Potential for Measurement Bias	Potential for Confounding	Important Results	Conclusions
<p>Colfax, G., Buchbinder, S., Vamshidar, G., et al., 2005.</p> <p>To describe participants' motivations for joining the first phase 3 HIV vaccine efficacy trial, the VAX004 trial, and to identify the demographic and behavioral correlates of study participation.</p>	<p>Cluster Double-Blind RCT</p> <p>61 sites, 57 in the U.S.</p> <p>Details of randomization process not given</p> <p>Study population were MSM and women at risk for heterosexual transmission</p>	<p><b>Moderate</b></p> <p>-Don't discuss how many excluded or ineligible</p> <p>- Recruitment methods varied by site</p> <p>-Selection criteria different for men vs. women (women may have been more "high risk")</p> <p>-Very few women enrolled</p>	<p><b>Minimal</b></p> <p>-Possible over-reporting of altruistic reasons or under-reporting of other reasons (non-differential)</p>	<p><b>Moderate</b></p> <p>-4% of men, but 55% of women were black</p> <p>-Adjusted for sociodemographic and sexual risk variables</p> <p>-Adjusted for study site</p> <p>-Don't know how well randomization worked</p>	<p>-Nearly all participants agreed or strongly agreed to participating for altruistic reasons.</p> <p>-3/4 joined to receive current info on HIV</p> <p>--1/2 joined to reduce their risk behavior or to get protection from HIV</p> <p>--1/2 joined for free HIV testing</p> <p>-Women were more likely than men to provide multiple reasons for joining</p> <p>-Women were stat. significantly more likely than men to agree or strongly agree with joining to receive free HIV testing, reduce risk behavior, for financial reimbursement, to obtain current information on HIV, and to get protection from HIV</p> <p>-After adjustment, sex and having 13 or more sex partners in past 6 months were associated with joining the trial for protection.</p> <p>-After adjustment, sex, unprotected anal or vaginal sex in past 6 months, 13 or more sex partners in past 6 months, and educational level were associated with joining trial to reduce risk. Race was nonsignificant (OR=2.0, 95%CI 1.0-4.4)</p> <p>-After adjustment, sex, race, 13 or more sex partners, and education were associated with joining for composite personal benefits.</p>	<p><b>Internal Validity: Fair</b></p> <p><b>External Validity:</b></p> <p><b>Generalizable primarily to U.S. MSM at high risk of HIV acquisition. Results are less generalizable to women and persons of color.</b></p> <p>Most participants joined for altruistic reasons, but many also joined to gain protection and to reduce their risk behavior.</p> <p>-Compared to non-HIV related studies, altruism appears to play a more important role in the decision to participate.</p> <p>-The most sexually active participants were strongly motivated by protection and least motivated by risk behavior reduction, despite having had pre-trial education.</p> <p>-Women and persons of color were more likely to report joining for multiple reasons, including receiving services. Additional public health efforts may be needed to ensure adequate access to these services outside of trials.</p>

## List of Figures

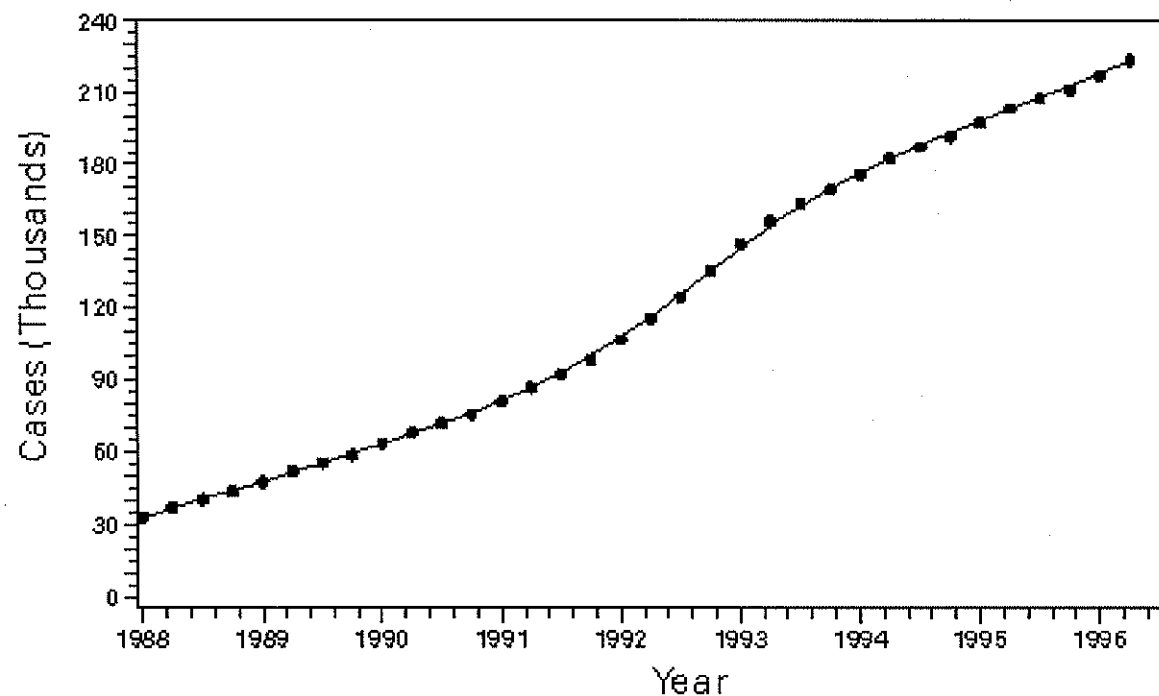
**FIGURE 1. Estimated AIDS incidence\*, deaths, and prevalence, by quarter-year of diagnosis/death — United States, 1981–2000**



\* Adjusted for reporting delays.

Figure 1. U.S. AIDS Incidence, Prevalence, and Mortality, 1981–2000 (CDC, 2001)

**FIGURE 5. Number of prevalent AIDS cases among persons aged  $\geq 13$  years, adjusted for delays in reporting, by quarter year — United States, 1988–June 1996\***



\*Points represent quarterly prevalence; the line represents "smoothed" prevalence. Estimates are not adjusted for incomplete reporting of diagnosed AIDS cases or AIDS deaths.

Figure 2. Taken from: CDC, 1997. MMWR, 46(08);165-173.



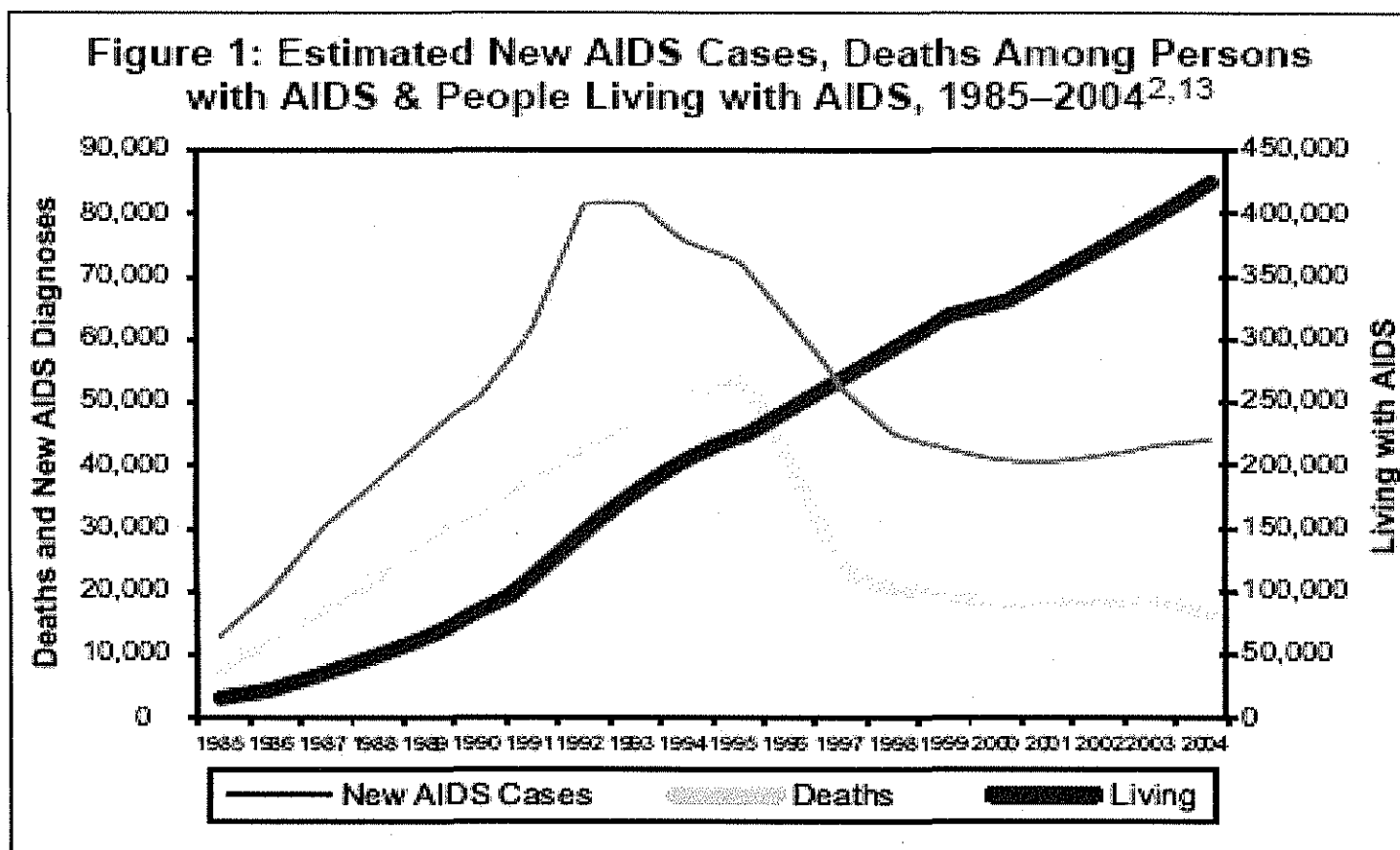
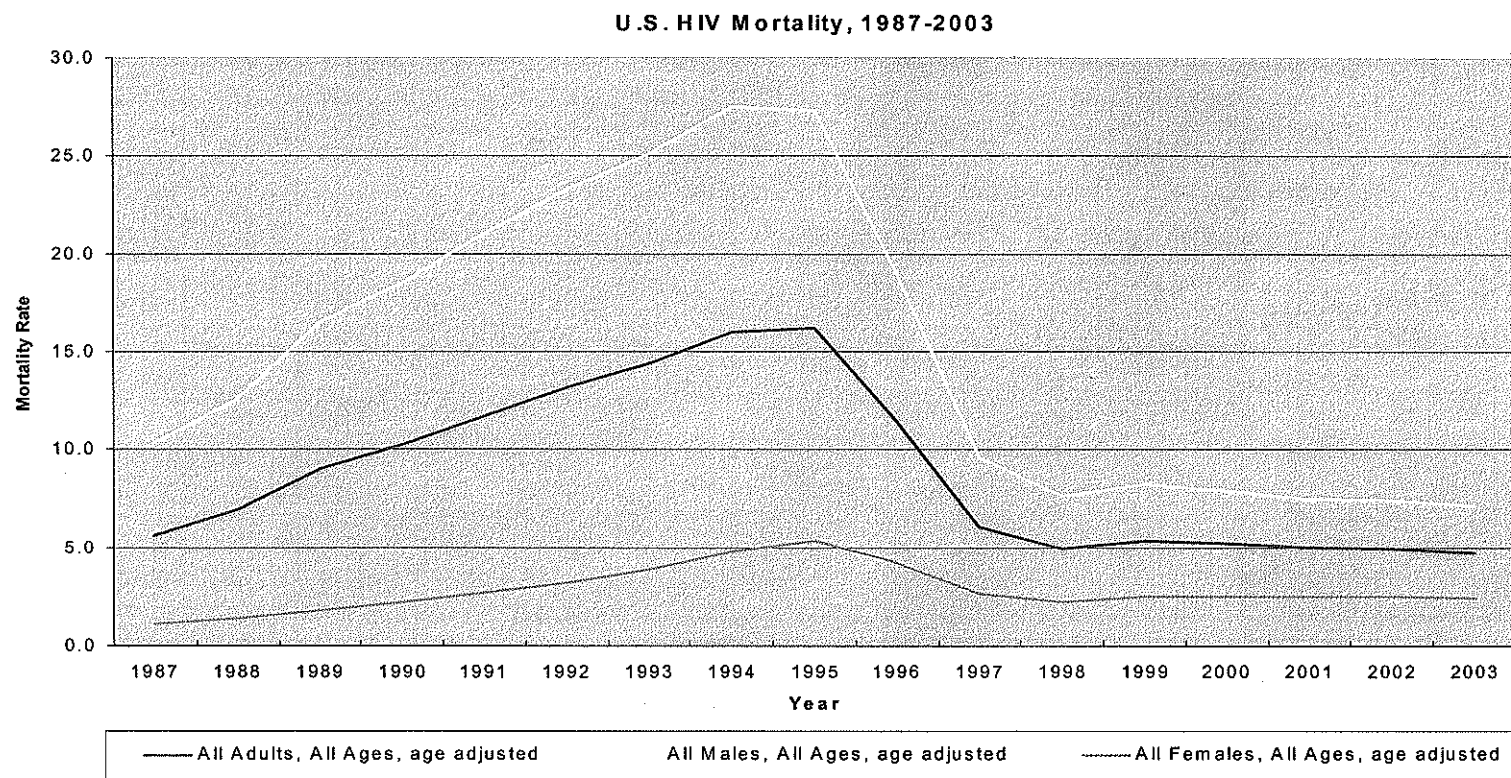


Figure 3. Taken from the HIV/AIDS Policy Fact Sheet. Kaiser Family Foundation, 2005. <http://www.kff.org/hivaids/upload/3029-06.pdf>

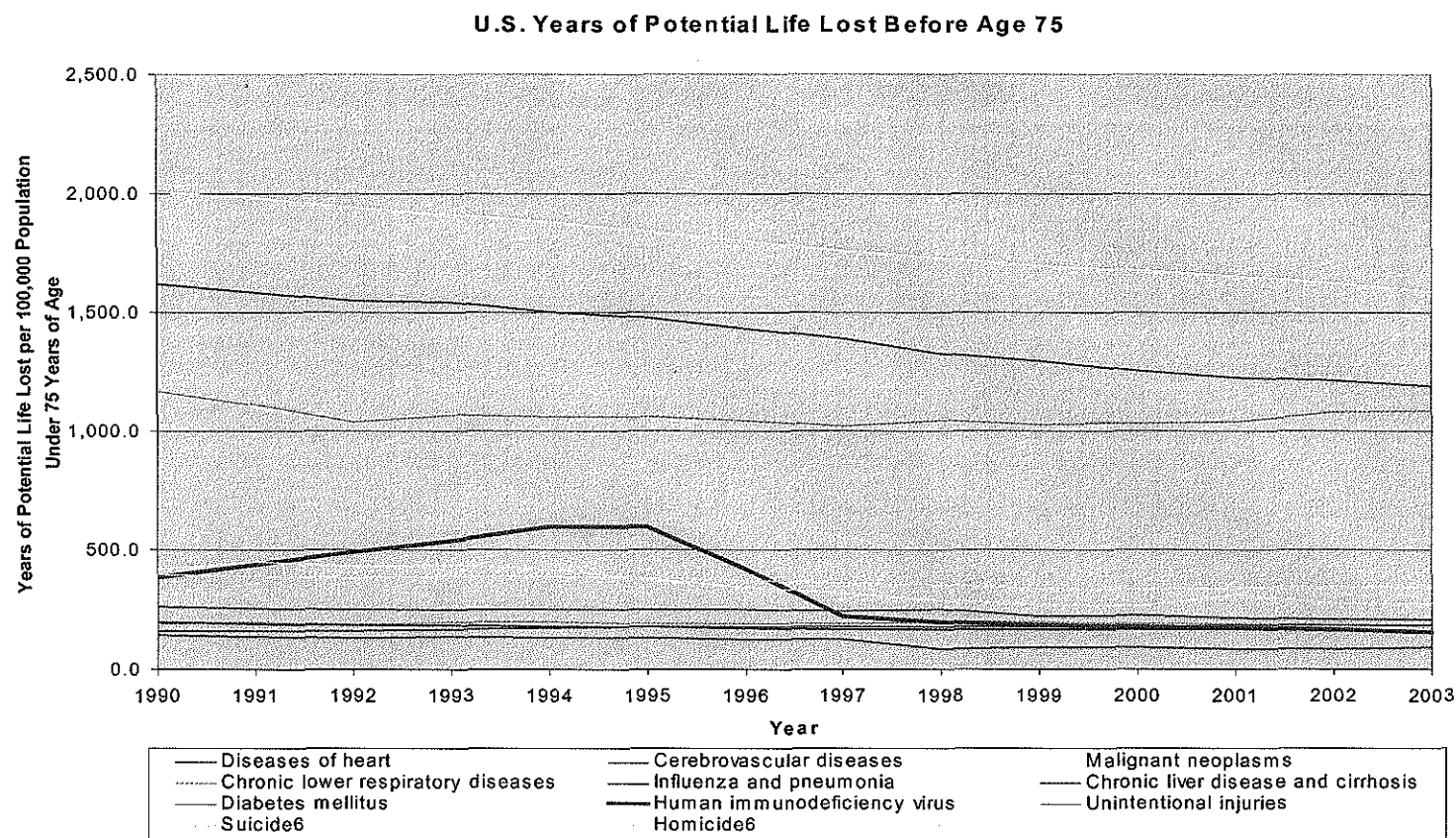
<http://www.cdc.gov/hiv/topics/surveillance/resources/slides/general/index.htm>



**Figure 5. Data for graph found in:**

**National Center for Health Statistics. Health, United States, 2005: With Chartbook on Trends in the Health of Americans.**

**Hyattsville, Maryland: 2005. <http://www.cdc.gov/nchs/data/hus/hus05.pdf>**



**Figure 6. Data for graph found in:**

**National Center for Health Statistics. Health, United States, 2005: With Chartbook on Trends in the Health of Americans**  
**Hyattsville, Maryland: 2005. <http://www.cdc.gov/nchs/data/hus/hus05.pdf>**

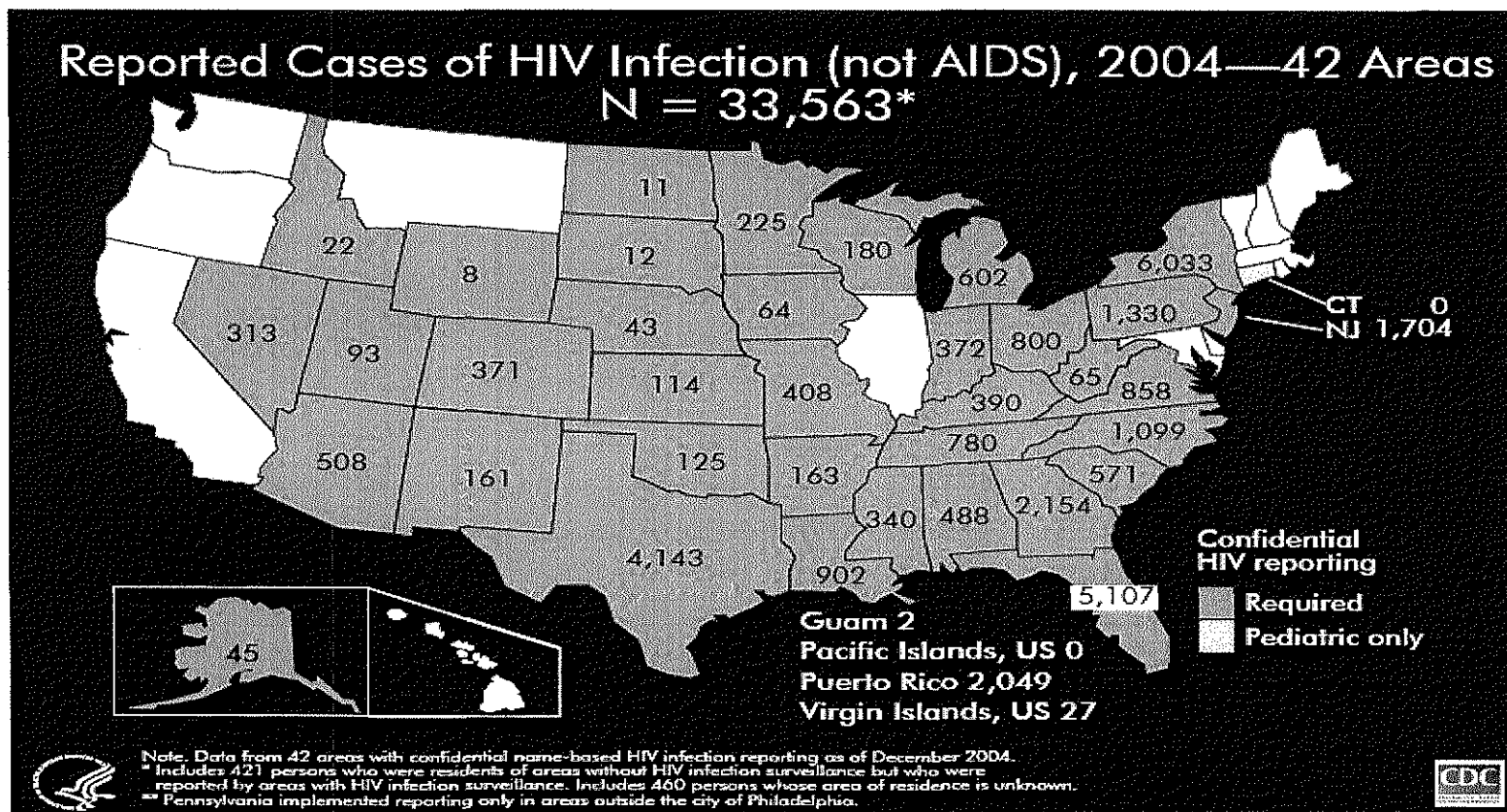


Figure 7. Figure taken from:

CDC, 2006. HIV/AIDS Surveillance - General Epidemiology (through 2004).  
<http://www.cdc.gov/hiv/topics/surveillance/resources/slides/general/index.htm>

# Estimated Prevalence Rates for Adults and Adolescents Living with HIV Infection (not AIDS), 2004—35 Areas

Estimated Prevalence Rates for Adults and Adolescents Living with HIV Infection (not AIDS), 2004—35 Areas

Rate (per 100,000 population)

- <100
- 100 - 150
- >150

Total rate=136.7

Note. Data from 35 areas with confidential name-based HIV infection reporting since at least 2000. Data have been adjusted for reporting delays.

CDC

Area	Rate (per 100,000 population)
Alaska	45.9
Arizona	114.5
California	162.3
Colorado	29.5
Connecticut	238.3
Delaware	147.5
District of Columbia	140
Florida	228.9
Georgia	139.3
Hawaii	125.3
Idaho	18.3
Illinois	20.4
Indiana	82.4
Iowa	15.0
Kansas	26.7
Kentucky	40
Louisiana	130.6
Maine	71.3
Massachusetts	208.5
Michigan	47.9
Minnesota	71.8
Mississippi	203.8
Missouri	98.3
Montana	15.0
Nebraska	42.0
Nevada	40.5
New Hampshire	71.3
New Jersey	208.5
New Mexico	56.0
New York	155.2
North Carolina	186.8
North Dakota	77.3
Ohio	94.8
Oklahoma	48.8
Oregon	150.6
Pennsylvania	130.6
Rhode Island	170.6
South Carolina	186.8
South Dakota	15.0
Tennessee	139.3
Texas	125.3
Vermont	71.3
Virginia	130.6
Washington	29.5
West Virginia	40
Wisconsin	20.4
Wyoming	15.0
Guam	47.8
Virgin Islands, US	281.7

**CDC, 2006. HIV/AIDS Surveillance - General Epidemiology (through 2004).**  
**<http://www.cdc.gov/hiv/topics/surveillance/resources/slides/general/index.htm>**

Figure 2.1. HIV disease reports over time

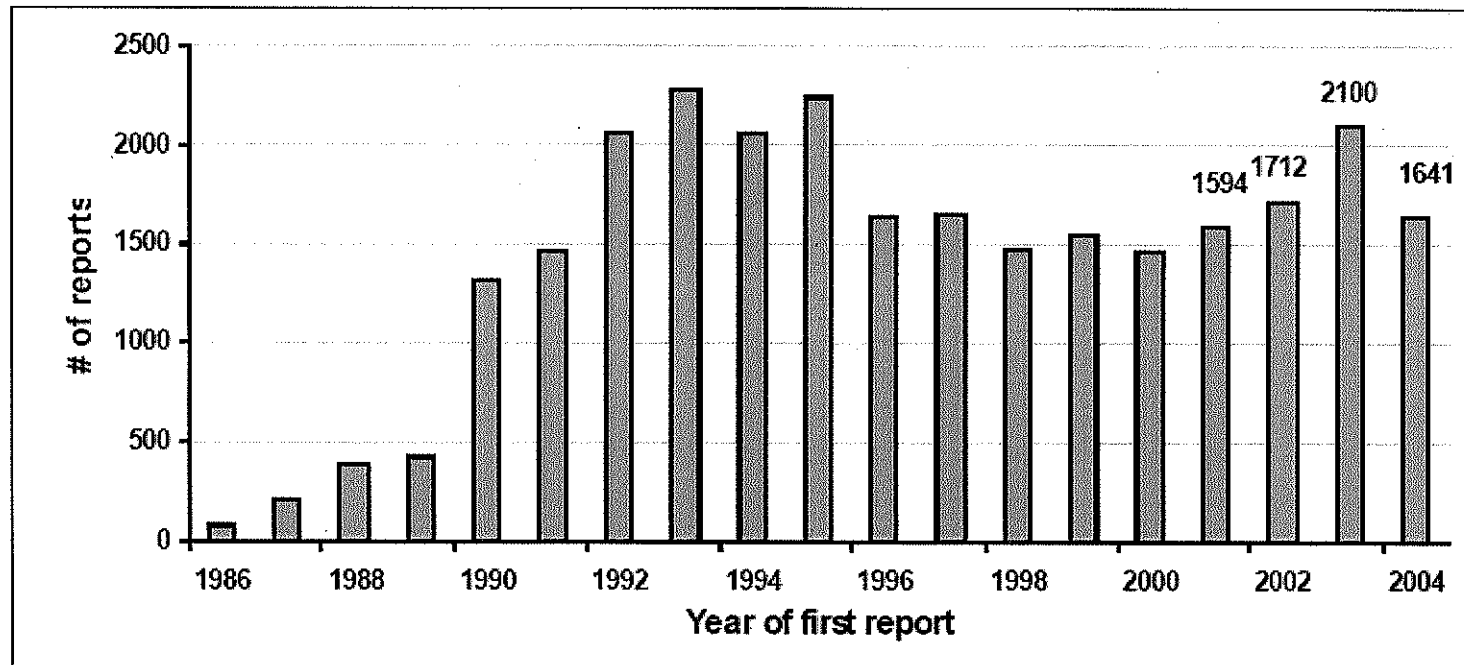


Figure 9. Graph

taken from: State of N.C., N.C. Dept. of Health & Human Services, Division of Public Health, 2005. North Carolina Epidemiologic Profile for HIV/STD Prevention & Care Planning. [www.dhhs.state.nc.us](http://www.dhhs.state.nc.us)

**Figure 2.2. Persons living with HIV in North Carolina, 2000-2004**

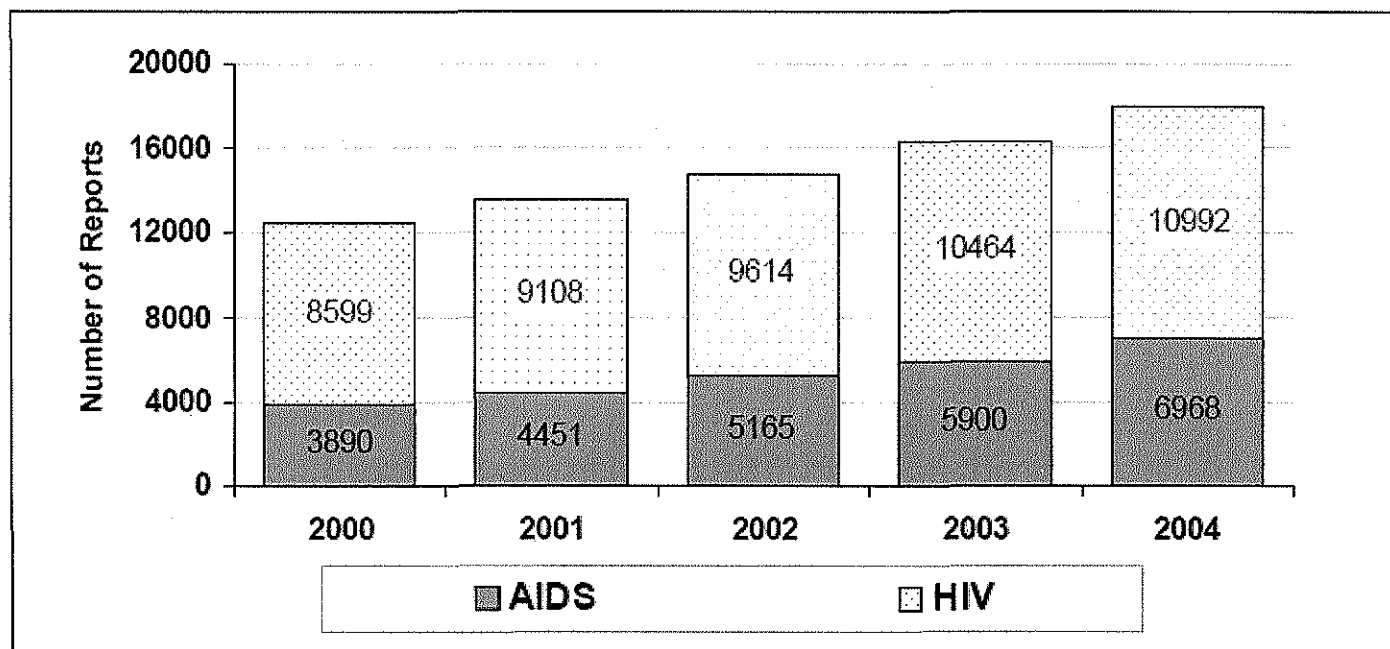
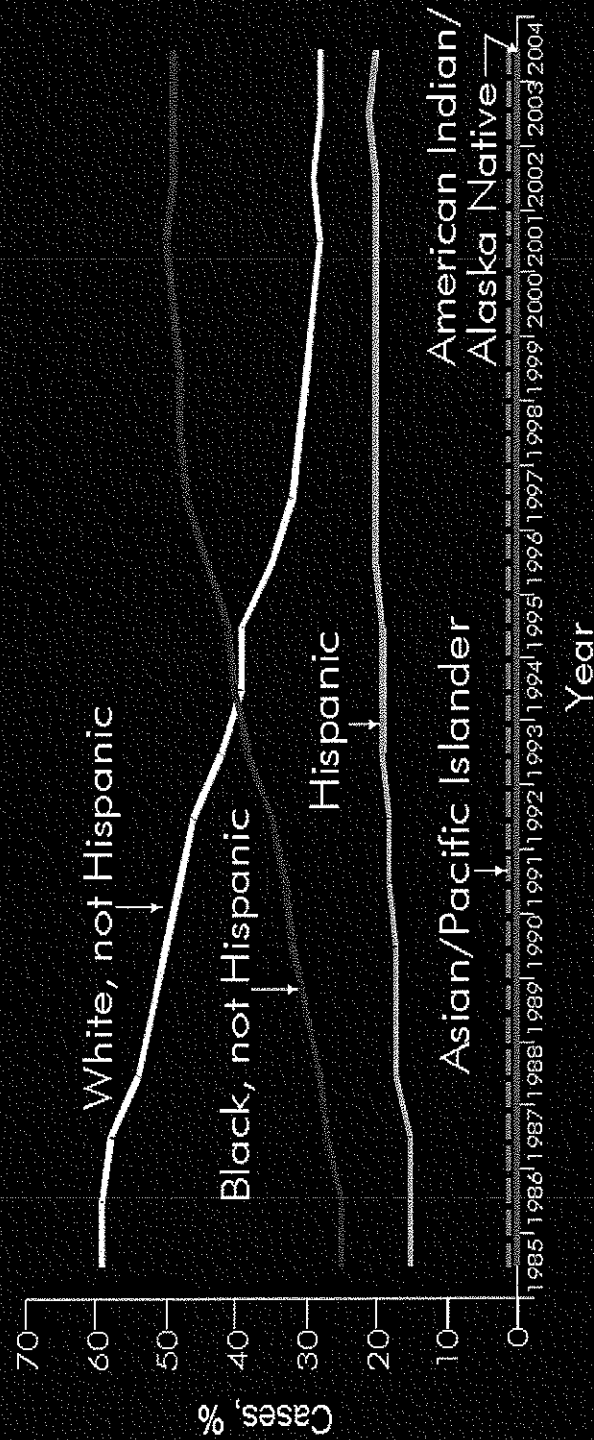


Figure 10. Graph taken from:

State of N.C., N.C. Dept. of Health & Human Services, Division of Public Health, 2005. North Carolina Epidemiologic Profile for HIV/STD Prevention & Care Planning. [www.dhhs.state.nc.us](http://www.dhhs.state.nc.us)

# Proportion of AIDS Cases among Adults and Adolescents, by Race/Ethnicity and Year of Diagnosis 1985–2004—United States



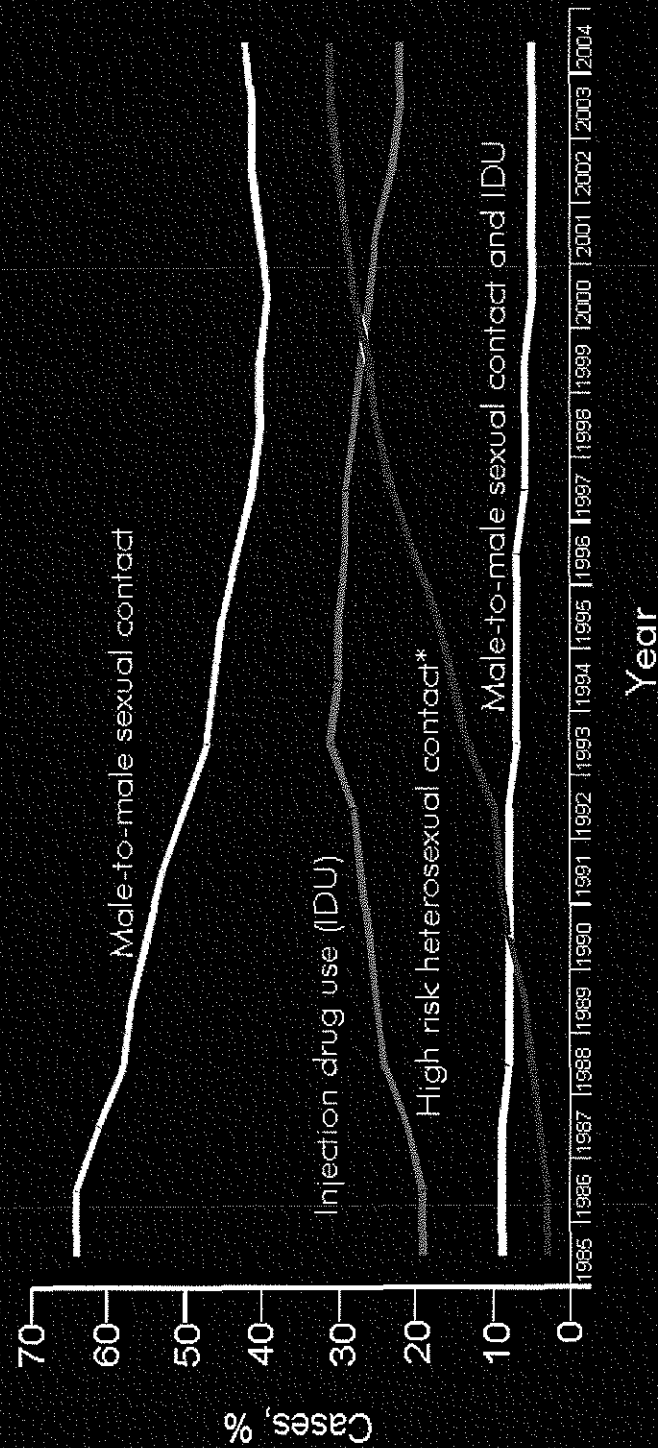
Note. Data adjusted for reporting delays.



Figure 11. CDC, 2004



# Proportion of AIDS Cases among Adults and Adolescents, by Transmission Category and Year of Diagnosis, 1985–2004—United States

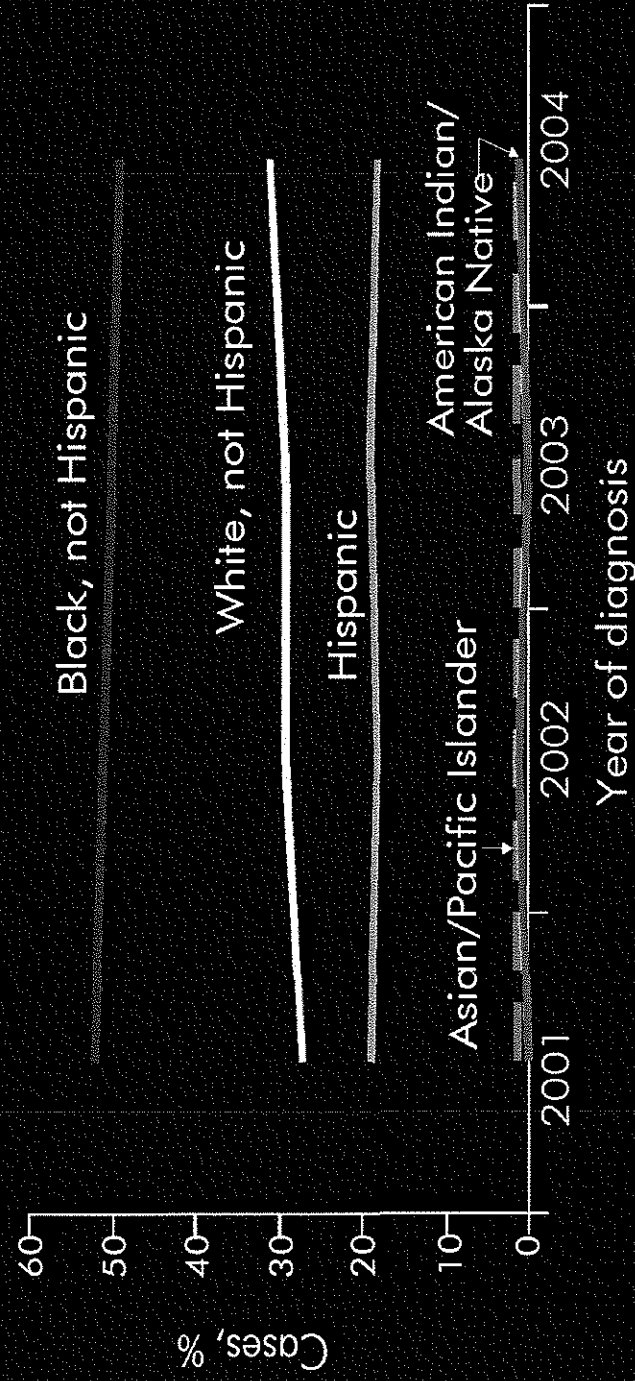


Note. Data adjusted for reporting delays and cases without risk factor information were proportionally redistributed.  
 \* Heterosexual contact with a person known to have or at high risk for HIV infection.



Figure 12. CDC, 2004

# Proportion of HIV/AIDS Cases among Adults and Adolescents, by Race/Ethnicity, 2001–2004—35 Areas

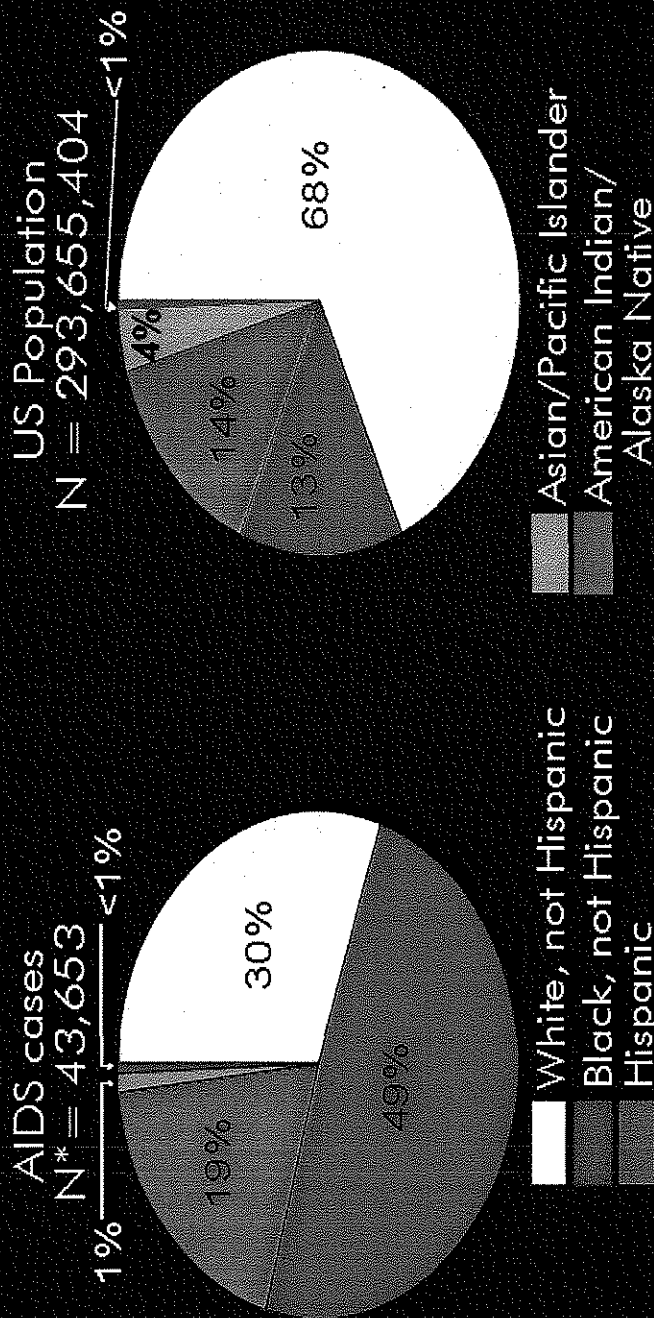


Note. Data include persons with a diagnosis of HIV infection regardless of their AIDS status at diagnosis. Data from 35 areas with confidential name-based HIV infection reporting since at least 2000. Data have been adjusted for reporting delays.



Figure 13. CDC, 2004

# Proportion of AIDS Cases and Population by Race/Ethnicity, Reported in 2004—50 States and D.C.

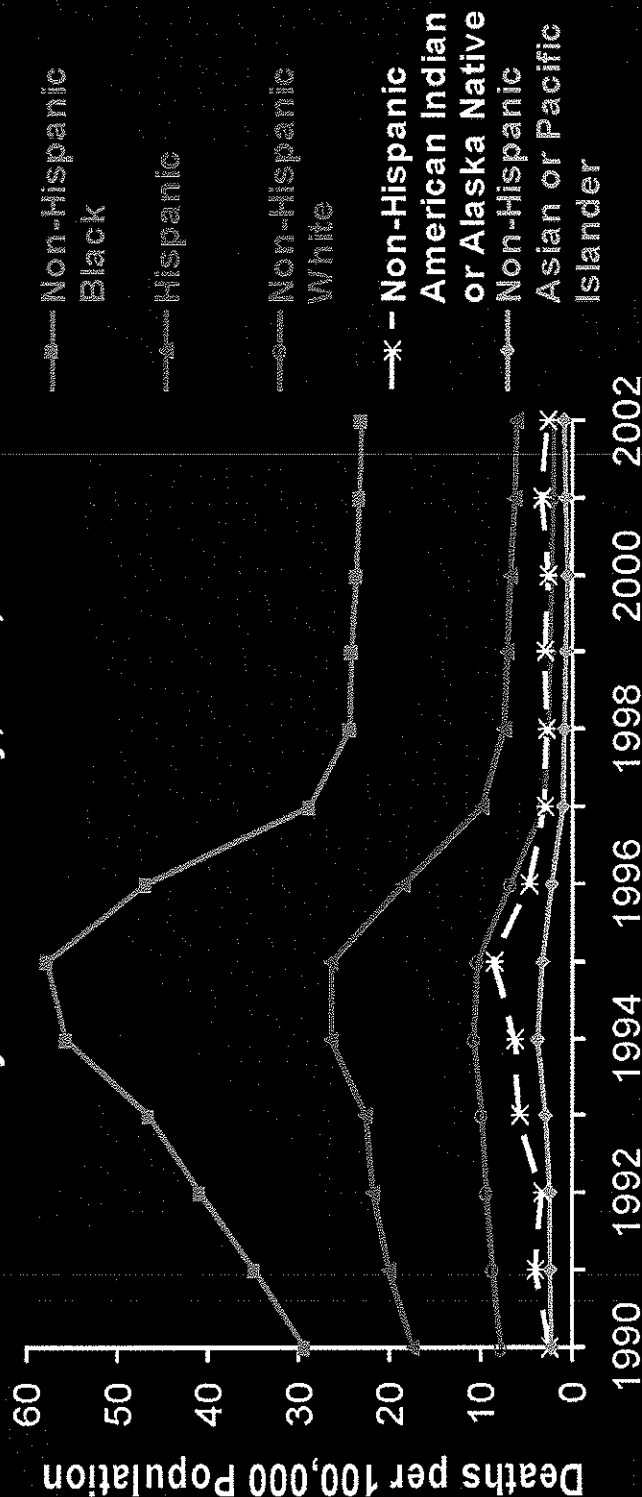


Note. Excludes persons from US dependencies, possessions, and associated nations.  
 \* Includes 191 persons of unknown race or multiple races.



Figure 14. CDC, 2004

# Trends in Age-Adjusted\* Annual Rates of Death due to HIV Disease by Race/Ethnicity, USA, 1990–2002



Note: For comparison with data for 1999 and later years, data for 1990–1998 were modified to account for ICD-10 rules instead of ICD-9 rules.

\*Standard: age distribution of 2000 US population



Figure 15. CDC, 2002

# Proportion of Persons Surviving, by Number of Months after AIDS Diagnosis during 1996–2003 and by Race/Ethnicity—United States

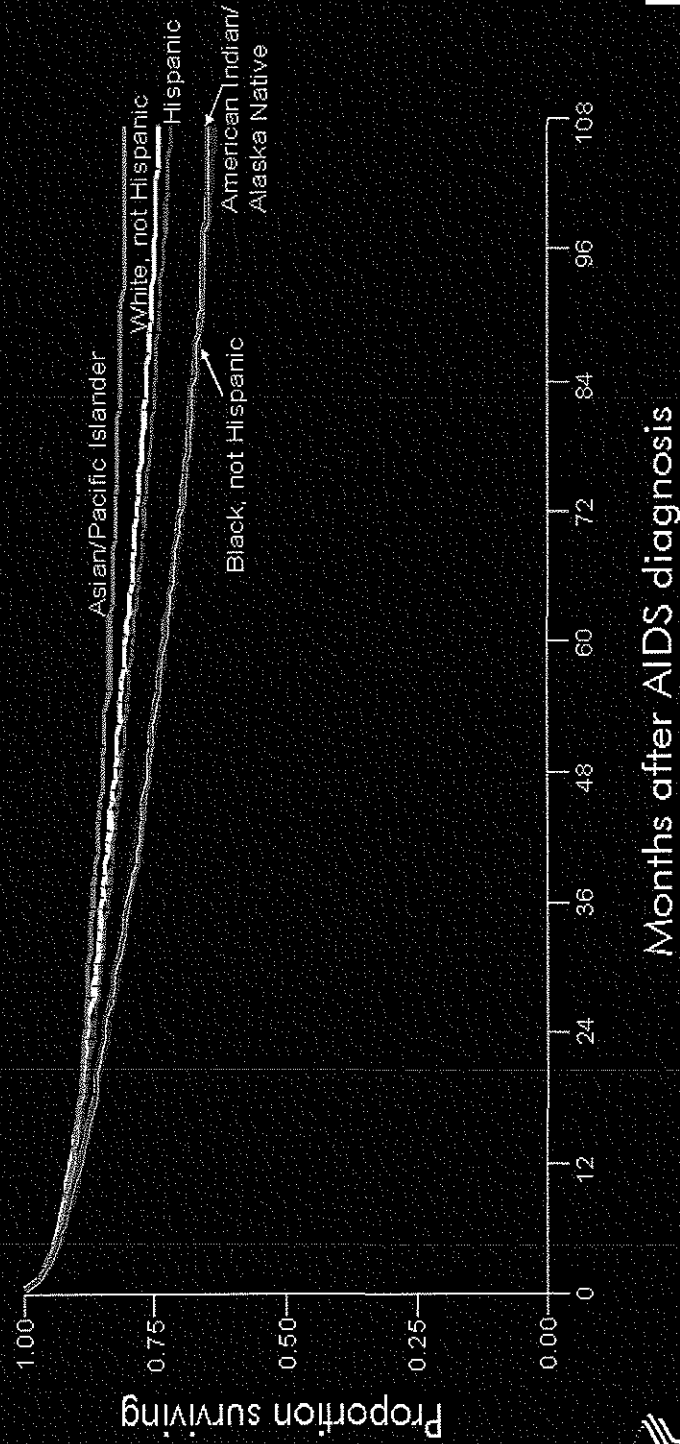
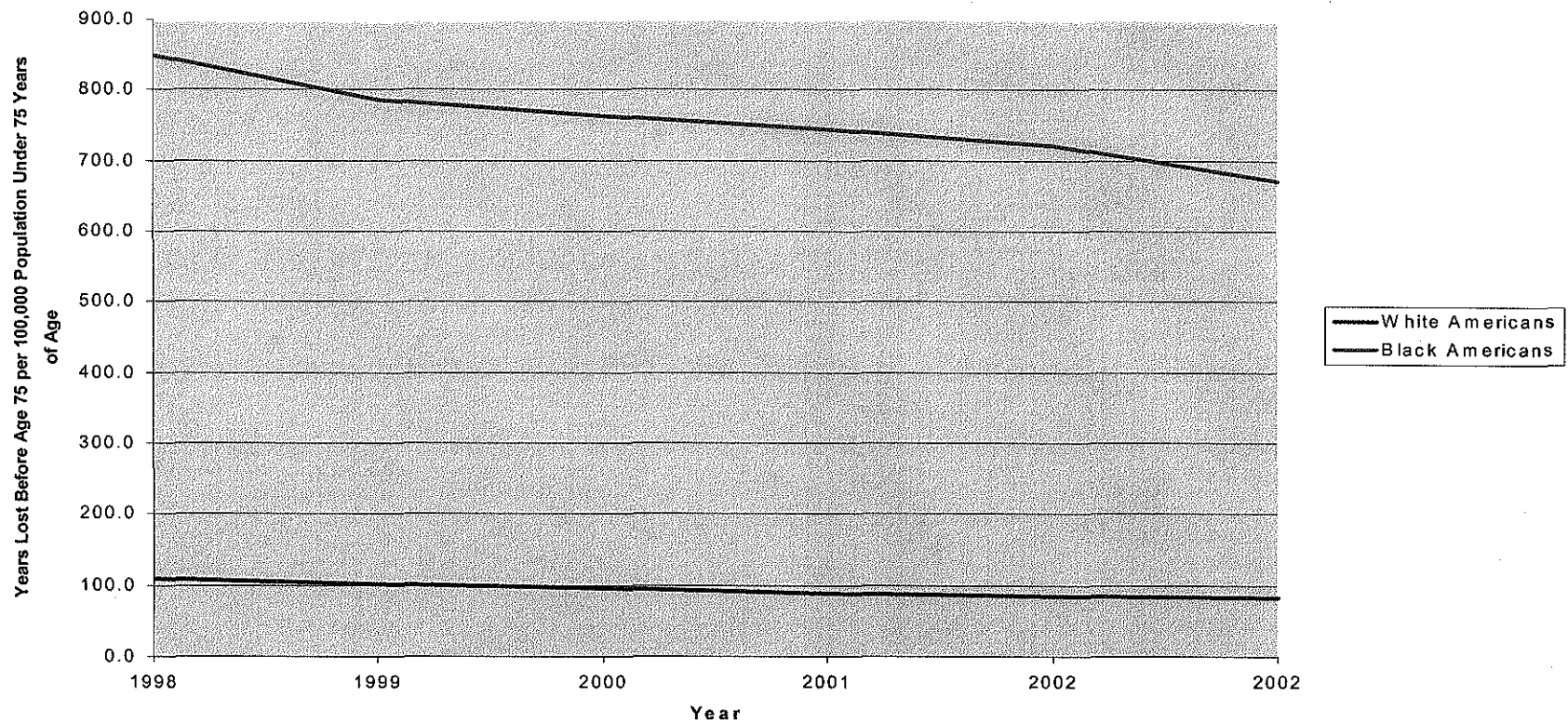


Figure 16. CDC, 2004

**U.S. Years of Potential Life Lost from HIV, by Race**



**Figure 17. U.S. Years of Potential Life Lost from HIV, by Race**

**Data for graph found in:**

**National Center for Health Statistics. Health, United States, 2005: With Chartbook on Trends in the Health of Americans**